The Cost of Survival:

Identifying Life Course Associations between Childhood and Adult Health Outcomes in the Skeletal Record.

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A thesis submitted in fulfilment of the

requirements for the degree of

Doctor of Philosophy

in Anthropology,

The University of Auckland, 2017

ABSTRACT

A central concern in adult health is understanding the role that early health experiences, such as during childhood, may play in shaping later adult health outcomes. The aim of my research is to employ a life course approach to investigate possible associations between health insults experienced in childhood, between two and six years, and health outcomes in adulthood. In addition, I will also examine if, and how, adult health outcomes might be mediated or modified through biosocial aspects such as sex and socioeconomic status.

This will be achieved through the analysis of human skeletal remains, involving the assessment of physiological stress indicators visible on both teeth and bone. Data are collected from 195 individuals from four London cemeteries spanning a range of socioeconomic positions and who lived during the Industrial Revolution (~1750 to 1850). Skeletal stress indicators associated with infancy and childhood, including cribra orbitalia and final long bone lengths, are used in conjunction with a dental indicator, enamel hypoplasia, which allows the frequency and timing of childhood health insults to be estimated. Adult health outcomes are assessed in term of periosteal new bone lesions, periodontitis, and age at death. These data are supplemented by parish burial records for two collections representing the highest and lowest socioeconomic groups (n = 9239).

Findings suggest that childhood health insults can influence adult health but not in the manner expected. Here, the predominant impact of early stressors was beneficial to adult survival and acquired immunity is suggested as a key factor in this association. This effect is more pronounced in higher SES groups and it is likely an accumulation of risks across the life course exerted a stronger influence on lower SES individuals.

ACKNOWLEDGMENTS

Many thanks to Judith Littleton (my main supervisor) for her unflinching support, determination, and guidance during this undertaking. Thank you to Bruce Floyd (my second supervisor) for his patience and careful attention to detail. Thanks to Caitlin Bonham Smith for always being happy to listen to my new ideas, as well as Mark Jones (my son), Drew Brown, and Ashley McGarry for kindly proof reading this work. I am indebted to Rebecca Redfern and Jelena Bekvalac at the Museum of London Centre for Human Bioarchaeology for their kind support and allowing access to their wonderful skeletal collections. I am also grateful to the University of Auckland Doctoral scholarship for funding three years of my life. And last, but certainly not least, I would like to thank Dave Maze (my husband) for his unwavering support in all matters and the many hours he spent transcribing burial records.

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CHAPTER ONE: INTRODUCTION

1.1 Introduction

A critical issue in adult health is understanding the role that subadult development may play in shaping later health. Although a growing body of research linking early life health experiences with later adverse health in adulthood supports the relevance of this issue (e.g. Barker and Osmond 1986; Bengtsson and Lindstrom 2000, 2003; Quaranta 2014), identifying individual connections between health events that are often separated by decades is especially difficult in long lived humans. One feature that has become apparent through these studies is that physiological stressors (such as disease and poor nutrition) occurring during particular stages of development may be more likely to have subsequent health costs. In certain environmental settings, for example, uterine stress is associated with later obesity and metabolic disturbances, such as type ll diabetes and cardiovascular disease, (Barker 2004; Cameron & Demerath 2002). In life course epidemiology, these vulnerable periods are referred to as either sensitive or critical periods of development, depending on whether the vulnerability is primarily driven by social or biological factors (Ben-Shlomo and Kuh 2002: Lynch and Smith 2005). Therefore, considering both the social and biological influences in early and later life is crucial to understanding how health is shaped across the life span.

To date, most research regarding vulnerable periods has focused on stress occurring during the early years of life and its relationship to later health. The Developmental Origins of Adult Health and Disease model, an extension of the Barker hypothesis, focuses research on the intrauterine environment including possible

pathways that connect early and later life health experiences (reviewed in Cameron & Demerath 2002; Ben-Shlomo and Kuh 2002; Myrskylä et al. 2014). Life course approaches have broadened the age focus to include childhood and adulthood, as well as intergenerational influences on health outcomes (Ben-Shlomo and Kuh 2002). However, the predominance of birth weight studies suggests that data relating to older children is more difficult to acquire. Research that has investigated associations between infant and childhood illness with later life disease suggests the timing of these initial insults may also influence subsequent health. For example, individuals exposed to inflammation or infections during the first year of life are more likely to experience chronic degenerative diseases and higher mortality rates in old age than those who were older at initial exposure (Bengtsson & Lindström 2003; Crimmins & Finch 2006). Identifying the timing of these vulnerable periods and their sequelae is central to understanding the role that childhood health can have across an individual's life.

Due to the relatively long human life span, however, identifying associations between childhood and later life health experiences is challenging. Relatively few studies have been able to utilise longitudinal data spanning from infancy or childhood into adulthood (for example, Bland and Jones 1951; Barker et al. 1989; Power and Peckham 1990; Shaheen et al. 1998; Berg et al. 2007; Margolis 2010). Animal models have been used as alternatives but they may reflect different developmental or life history pathways to humans and are not always appropriate for aspects of human physiology (Sinclair et al. 2007; Nijland et al. 2008; Wynne et al. 2011). Other studies have relied on retrospective analyses where older adults are asked to recall childhood health experiences, but these are subject to recall bias and may be incomplete (Blackwell et al. 2001; Lynch and Smith 2005; McEniry 2011). Population level analyses following year of birth cohorts can detect correlations between higher rates of

childhood mortality, which imply higher levels of disease exposure and morbidity, with increased mortality rates in those who survived to adulthood (Bengtsson and Lindström 2003; Buck and Simpson 1982; Catalano and Bruckner 2006; Crimmins and Finch 2006; Myrskylä 2010). Population level data, however, does not allow direct associations between the early and later health outcomes. In order to establish direct connections, information on early stress episodes together with later health consequences are needed at the individual level.

Skeletal and dental analyses of human skeletal remains can allow relationships between childhood stress episodes and longevity to be identified in individuals. Episodes of childhood stress can leave a record in dental enamel, evident as enamel hypoplasia. These defects are not specific in nature so the precise cause of stress is usually unknowable. Nevertheless, they indicate that a systemic perturbation occurred that was severe enough to cause an interruption to enamel formation (Goodman & Rose 1990). Numerous studies have established links between enamel hypoplasia and episodes of under nutrition and disease (Nikiforuk & Fraser 1981; Suckling et al. 1983; Goodman et al. 1991; May et al. 1993; Seow et al. 1996; Brook and Smith 1998; Littleton 2005; Littleton and Townsend 2005), supporting their use as a reliable gauge of physiological stress. Furthermore, a particularly useful and unique aspect of enamel hypoplasia is the age of occurrence of these defects can be accurately estimated, due to the chronological nature of enamel formation. This means that unworn adult dentition retains a record of physiological stressors experienced during childhood, including the age of the individual when they experienced the insult.

A central question concerning associations between childhood stressors and adult health outcomes is whether the frequency of insults or the age when they occurred might have most impact. For example, is insult timing more likely to have lifelong

consequences compared to the sheer number of insults experienced during childhood, or do they work together to worsen outcomes? Analysing the timing of enamel hypoplasia allows these factors to be untangled, including when and how subsequent health outcomes might vary. A further aspect that needs to be considered is whether these associations might be mediated by socioeconomic status, as some work has suggested (e.g. Palubeckaite et al. 2002; Amoroso et al. 2014). It also needs to be remembered that age at death is a crude indicator of adverse health, rather than a nuanced gauge of morbidity. It is always possible that people may live longer but not be particularly healthy, especially in groups that have better access to health care and resources. Therefore, considering how socioeconomic position and sex may modify impacts or mediate outcomes of early stressors is essential to identifying sensitive or critical developmental periods in the skeletal record.

Morbidity cannot be reliably assessed in skeletal remains, as relatively few diseases leave bony lesions, and those that do will tend to be chronic in nature. Certain skeletal lesions, however, such as periosteal new bone formation and periodontitis, record occurrences of inflammation where surrounding tissue has been involved. Periosteal new bone formation is caused by the periosteum reacting to inflammation, resulting from a number of potential causes, such a trauma or infectious agents (Weston 2008), but which has been linked to an increased risk of death (DeWitte 2014). Periodontitis is an oral pathology caused by inflammation affecting the alveolar bone immediately surrounding the dental sockets. A growing number of studies link periodontitis with chronic health conditions, such as diabetes and coronary disease (Nelson et al. 1990; Naugle et al. 1998; Morrison et al. 1999; Garcia et al. 2001; Scannapieco et al. 2003a). These inflammatory indicators may help to assess if individuals who lived longer experienced chronic health conditions, which may be

particularly important in higher status groups where impacts of childhood health may be more subtle than indicated by age at death.

1.2 Aims

The aim of this research is to employ a life course approach to understand ways that childhood health may impact the adult through analysing skeletal and dental markers of adverse health. This involves identifying situations when childhood episodes of physiological stress appear to contribute towards later indications of adverse health in adulthood. Enamel hypoplasia provides information on the occurrence and timing of childhood stress episodes, and I include a novel method to estimate original height of worn crowns, allowing a greater degree of accuracy regarding defect timing. Age at death is used as the main indicator of adverse adult health, but periodontitis and periosteal new bone lesions also provide additional information on morbidity. Because health risks can vary by sex (Bouman et al. 2005), males and females are analysed separately. How early health insults might alter the risk of death or morbidity in adulthood is key to identifying how health is linked across the life span.

A biocultural approach is essential for understanding how social environments may mediate between early health insults and subsequent impacts. Therefore, individuals have been sourced from four cemetery collections of post medieval Londoners (18^{th} and 19^{th} centuries), which span high to low social groups, but all of who lived during major social changes elicited by the industrial revolution. Prior to assessing direct connections between early and later health outcomes, information on the general environments experienced by the differing socioeconomic groups during both childhood and adulthood is explored. This is to understand how their environments

may have differed in terms of health stressors as well as the scale of these differences. The childhood environments are assessed using skeletal indicators associated with disease and nutritional inadequacies, including porotic hyperostosis, cribra orbitalia, and long bone length, while the adult environments are investigated using periosteal new bone formation, periodontitis, and age at death. The underlying relationship between the distribution of mortality and the cause of death can also be understood by analysing the parish burial records for two of the collections representing the highest and lowest socioeconomic circumstances. By collating information from multiple sources, I will employ a ‘‘context-embedded’’ approach, as suggested by Klaus and Tam (2009), permitting the interpretation of biological stress indicators to be positioned within their relevant historical context.

Understanding the impacts that childhood health can have across an individual's lifespan serves to further elucidate factors influencing adult health and disease (Dietert et al. 2000; Cameron and Demerath 2002). Identifying associations linking childhood stress to adverse adult health is of primary importance, as is the identification of potential ages of vulnerability when stress may contribute more strongly to later disease. In addressing health patterns that span the life course, dental and skeletal analysis offers an additional longitudinal approach because it allows the ages when an individual experienced childhood stressors to be related to indicators of adult health at an individual level. By incorporating a biocultural approach, this thesis builds upon a significant body of research that has sought to understand the long term impacts of childhood stress (including but not limited to: Kermack et al. 1934; Bland and Jones 1951; Buck and Simpson 1982; Barker and Osmond 1986; Power and Peckham 1990; Shaheen et al. 1998; Bengtsson and Lindstrom 2000; Blackwell et al. 200; Ben-Shlomo and Kuh 2002; Cameron & Demerath 2002; Margolis 2003; Gluckman et al. 2005;

Floyd and Littleton 2006; Catalano and Bruckner 2006; Crimmins & Finch 2006; Berg et al. 2007; Myrskylä 2010; Quaranta 2014) and will endeavour to explain apparent variation in health outcomes.

CHAPTER TWO: A LIFE COURSE APPROACH TO HEALTH

2.1 Introduction

Central to this thesis is one fundamental question: in what circumstances might childhood health experiences impact adult health? Implicit to this question is the relevance of frequency and timing of health insults occurring during childhood and whether the relationship between early and later health might shift by sex or be modified by social factors. This chapter considers a body of research that has clearly established links between early and later life health. From initial studies focusing on stressors during very early life, life course epidemiology evolved to consider a broader range of both critical ages and types of stressors that might act across the life span. Although studies suggest that stressors operating well into childhood may still link to later disease risks (Fridlizius 1989; Blackwell et al. 2001; Crimmins and Finch 2006; Margolis 2010; Myrskylä 2010), this age group remains relatively underexplored. Developmental stages for the first ten years of life are outlined as competing demands between growth velocity, dietary transitions and immune development may create windows of increased susceptibility to infection and physiological disruptions, suggesting periods when health insults are particularly likely to influence later health. Useful life course models are described suggesting pathways and mechanisms that link health experiences across the lifespan including how social factors can interact with physiological impacts to create variation in outcomes (Preston et al. 1998; Ben-Shlomo and Kuh 2002). The chapter concludes with a model explaining how associations

between early stressors and later health outcomes might be detected in the skeletal record.

A life course approach considers how multiple factors, including biological, socioeconomic, and psychosocial, can act and interact to influence adult health. Broadly, it considers "the individual at any point in time as the sum of previous life experiences" (Agarwal 2016:131). Life course epidemiology offers conceptual models that suggest pathways linking early and later life health experiences, while mechanistic models have been proposed that recognise and interpret sometimes contradictory outcomes. These include influences such as scarring and selection that can shape mortality profiles and expose heterogeneous levels of frailty. Socioeconomic status is a broad measure of multiple factors that collectively describe an individual's position in the social hierarchy, which in turn is linked to their ability to access resources, such as adequate nutrition and housing, health care, and education (Elo 2009). While factors used to assess socioeconomic position may vary in relevance through time and place, the measure provides a useful way to understand how social inequalities can influence health and mortality (Elo 2009). Importantly, a life course approach considers how socioeconomic status, and therefore access to resources, might mediate or modify pathways and linking mechanisms, allowing a biocultural lens through which to explore health experiences and outcomes that cross life times.

2.2 A life course approach to adult disease

A seminal study that first noticed mortality rates across the life course often reflected childhood rates, led the authors Kermack, McKendrick and McKinlay (1934) to suggest that childhood health might impact later adult health. Utilising population

mortality data from Britain and Sweden, the authors reported consistencies in mortality rates such that cohorts that experienced high infant and childhood mortality rates experienced relatively higher mortality rates throughout their lives (Kermack et al. 1934). Later research from Norway suggested socioeconomic conditions during the early environment appeared to influence the risk arteriosclerotic heart disease in adulthood, especially when there was a later improvement in living conditions (Forsdahl 1978). The concept that health during the early years of life may influence adult health status brought a greater realisation of the importance of improved health care and nutrition for infants and children (Barker 2003; Finch and Crimmins 2004). The increase in life expectancy during the late 20th century in Westernized nations is suggested to reflect improved child health care policies implemented decades earlier, including a reduction in childhood infection and inflammation (Barker 2003; Finch and Crimmins 2004).

Some research suggested a mismatch between the early and later life environments may play a role in later disease development (Barker and Osmond 1986; Barker et al. 1989; Gluckman 2004; Gluckman et al. 2005). Implicit to the concept of mismatched environments underlying certain later health conditions is recognition that growth and development progress along trajectories established in early life (Gluckman 2004; Halfon et al. 2014). Incorporated within this concept is recognition that early development may be plastic, responsive to the environment in which it is shaped (Gluckman 2004; Halfon et al. 2014). Thus, the environment experienced during early life may result in subsequent development ideally suited to early conditions. If the later environment, however, is not matched to the earlier one, the individual may not be well suited and suffer adverse health as a result. Mismatched environments were suggested as causal in a study noting impoverished early life environments and high rates of

chronic health conditions in adulthood (Barker and Osmond 1986). The highest mortality rates for cardiovascular disease as well as bronchitis and stomach cancer, were in regions that had had the highest infant mortality rates approximately 50-70 years earlier (Barker and Osmond 1986), a finding similar to Forsdahl's Norwegian study (1978). This was in addition to the relationship between rising rates of heart disease and increased living standards. The authors concluded that poor nutrition in the early years of life may have predisposed individuals to these later disease occurrences when there had been a subsequent improvement in food availability (Forsdahl 1978; Barker and Osmond 1986).

Studies also found the timing of early stressors produced variable outcomes. For example, work investigating the timing of nutritional stress due to the Dutch famine of 1944–45 found that exposure during the last trimester of gestation and early infancy corresponded with lower obesity rates at nineteen years of age, while exposure during the first half of gestation had higher rates (Ravelli et al. 1976). In a British study, strokes in later life were associated with higher levels of foetal stress but not postnatal stress, while chronic bronchitis was only associated with an adverse postnatal environment (Barker et al. 1989). High rates of ischaemic heart disease were found in regions that had experienced high rates of either neonatal or infant mortality (Barker et al. 1989). These studies demonstrate links between early life and later life health but also suggest that stress occurring at different ages, or stages of development, may play out differently. Barker's (1990) research suggesting the role of the intrauterine environment in the subsequent development of adult disease led to the formation of what became known as the Barker hypothesis. These associations were substantiated by later studies utilizing individual records, which allowed direct connections between neonatal and postnatal health, including birth weight, weight at one year, and feeding

practices, to be linked to mortality, including specific diseases (Syddall et al. 2005; Barker 2003).

Since its inception, Barker's hypothesis, or the foetal origins of adult disease (FOAD) hypothesis, has been redefined several times, including the foetal programming hypothesis, the intrauterine growth restriction hypothesis, and the thrifty phenotype. Further, in recognition of the important influences of postnatal development, the model was broadened by Gluckman and Hanson (2006) to the Developmental Origins of Health and Disease, or DOHaD. These models focused research on the relationship between later adult health and the early stages of life involving the uterine and early neonatal environments, with particular attention to chronic adult disease conditions (De Boo and Harding 2006; Innis 2011; Kuzawa and Quinn 2009; Nijland et al. 2008; Woroniecki et al. 2011), but also increased risks of various infectious diseases, autoimmune diseases, and cancers (Elo and Preston 1992; Yabuhara et al. 1997; Hall et al. 2002).

Research investigating subsequent impacts of infant and childhood stress suggests that exposure to infectious disease during this period can also carry a delayed cost realised in adulthood (Fridlizius 1989; Shaheen et al. 1998; Bengtsson and Lindstrom 2000, 2003; Catalano and Bruckner 2006; Bruckner and Catalano 2009; Margolis 2010; Quaranta 2014). For example, American birth cohorts with greater exposure to diarrhoea and enteritis during infancy were at greater risk of death from heart disease or respiratory cancer in old age (Buck and Simpson 1982). A number of Swedish cohort studies have reported increased adult mortality rates for individuals who experienced greater exposure to infectious diseases during early childhood (Fridlizius 1989; Bengtsson and Lindstrom 2000, 2003), while a Scottish cohort study found impaired lung capacity in old age was linked to respiratory infections

experienced during the first two years of life (Shaheen et al. 1998). In addition, a study utilizing longitudinal data from Guatemala found rates of childhood illness (grouped as diarrhea, anorexia, fever, infectious diseases, and serious illnesses) were positively associated with developing later risks of cardiovascular disease, but the strongest predictor of adult morbidity was intense periods of illness during early childhood (1 – 2 years old) combined with recurrences in later childhood (Margolis 2010).

Historical work with Swedish, Danish, English, and Welsh cohorts suggested the subsequent ages when mortality appears most impacted by early childhood disease exposure may also vary, with some cohorts experiencing greatest mortality prior to adulthood during adolescence, while for others, the toll is exerted during adulthood (Catalano and Bruckner 2006; Bruckner and Catalano 2009). Further work has pointed to sex differences in the ages when individuals are at most risk of death from early disease exposures. A Swedish cohort study found that female mortality risk was highest during older adulthood, specifically those older than 44 years, while the male risk was generally higher, but greatest between 20 to approximately 50 years (Quaranta 2014). Other work investigating survivors of the Great Chinese Famine (1959–1961) suggests adult consequences that vary by sex may be due to either biological or cultural influences (Mu and Zhang 2011). These studies point to exogenous stressors experienced during infancy and early childhood as being able to exert a toll on later adult health. Furthermore, variation in the later ages when this toll is operational may be influenced by sex as well as social behaviours. Thus, developmental trajectories may also be established, and altered, by social influences impacting behaviour and health across the life course (Halfon et al. 2014).

Life course approaches to adult health have also benefited from studies of past peoples. Work by Agarwal and Grynpas (2009) found that age related patterns in bone

density loss likely differed in past populations compared to modern, suggesting that osteoporosis is unlikely to only reflect hormonal changes associated with menopause. Further work highlights bone maintenance and loss as a dynamic process operating across the life course, influenced by numerous factors including diet, parity, and life style factors, often acting from early in life (Agarwal and Beauchesne 2011). A life course approach was used to explore the influence of socioeconomic status on associations between childhood health insults (enamel hypoplasia) and age at death in an historic Portuguese sample (Amoroso et al. 2014). These results suggested that the accumulation of adverse socioeconomic risks may have a greater influence on adult survival than childhood health insults (Amoroso et al. 2014). More recently, a life course perspective was employed to investigate variation between males and females in occurrences of childhood health insults, evidenced by pathological striae in internal enamel, and subsequent adult survival in a medieval Danish population (Gamble et al. 2017). Their findings suggest a dimorphic response with adult male survival negatively influenced by early stressors while females experienced increased survival (Gamble et al. 2017). Other times, life course approaches are used in bioarchaeology but not always implicitly. One study, for example, used multiple skeletal stress indicators operating at different subadult ages to investigate health impacts associated with social and economic change before and after 1700 in northern England (Watts 2013). This work suggested that improved economic conditions can alter how early stressors impact adult mortality (Watts 2013).

In general, this body of research indicates that in addition to the foetal and neonatal environment, stressors - particularly infectious disease, experienced during infancy and childhood - can also impact adult health. However, although age periods are divided into pre and postnatal stages, including neonates and infants up to one or

two years of age, the ages that collectively define childhood are usually three to seven years (Bogin 1997) and grouped as a single life stage, despite this covering approximately five years of development. Yet the relatively few studies that do include childhood suggest stressors during this phase can still impact adult health (e.g. Kermack et al. 1934; Forsdahl 1978; Fridlizius 1989; Shaheen et al. 1998; Margolis 2010; Quaranta 2014). Another consideration is that in addition to specific timing, socioeconomic status is often not available in many studies so its impact on health outcomes is not always testable (but see exceptions, Preston et al. 1998, Bengtsson and Broström 2009).

2.3 Sources of life course data

The lack of information on stressor timing within childhood is likely due to the type of the data often available for analysis, which may rely on proxies for childhood exposures, such as mortality rates, or retrospective data, making it difficult to pinpoint possible vulnerable ages linked to adult disease (Bruckner and Catalano 2009; Margolis 2010). Furthermore, researchers may lack information regarding practices such as weaning or socioeconomic position, rendering it difficult to determine how these may influence outcomes. It is known, however, that both these factors play influential roles on disease exposure and susceptibility as well as ability to recover (Cunningham et al. 1991; Preston et al. 1998; Kuh et al 2004; Hanson 2007; M'Rabet et al. 2008). In addition, there may be no obvious connection between disease in adulthood and stressors experienced decades before, making these periods particularly challenging to detect.

When researchers rely on historical records, their variables are limited to data recorded at the time rather than what might be the most meaningful for their particular study. For example, low birth weight has often been used as a proxy for foetal growth and the intrauterine environment but is only a broad measure. As a single measurement, birth weight can be confounded by gestational age: a neonate may be premature but still have a healthy weight for its gestational age. Although this can be resolved by including data on gestational age, such data are rarely available historically. Furthermore, population level data such as infant mortality rates may be useful proxies when read at the population level (for example, to infer likelihood of disease exposure), but do not allow meaningful inferences to be made about an individual, and to do so is to commit the ecological fallacy (Robinson 2009). Although population level data will allow trends and correlations to be detected, identifying actual 'cause and effect' relationships can only be done with individual level data. However, this level of data on early health experiences can be difficult to obtain; it may be necessary to rely on participants' own recollections of childhood health experiences. For example, Blackwell et al. (2001) related childhood episodes of illness, recounted by elderly participants, to coronary heart disease in later life. The concern is that this method can introduce considerable bias as the ability to accurately remember early life events may not be equal amongst participants (Margolis 2010).

Animal studies offer another avenue for life course research and have the advantage of being able to demonstrate direct cause and effect through controlled experiments. For example, murine studies have demonstrated that exposure to immunotoxic chemicals during early life is related to the development of autoimmune diseases in later life (Holladay & Smialowicz 2000). Yet, animal models do not always behave or respond to stressors in the way humans might (Carter 2007). Concern has

been expressed at the low rate (approximately one third) of translation between experimental animal findings and human clinical outcomes for a wide range of diseases, including both chronic and acute conditions, possibly due to animal models failing to adequately simulate human disease outcomes (Hackam and Redelmeier 2006; Hackam 2007; Perel et al. 2007; Sclafani 1984; van der Worp et al. 2010). Humans experience a greater amount of postnatal growth, particularly brain development, and demonstrate a unique pattern of growth compared to other mammals so may vary in the timing of critical periods due to relative differences in the development stages of organs and systems (Bogin 1999). While animal studies are useful in pointing to stages of development when exposure to stressors are likely influential to later health, they may not afford detailed timing within the period of childhood development that is unique to humans. This can hinder a life course approach as stressor timing is a particularly relevant component in models used to understand life course connections. By allowing the frequency and timing of early health insults to be established in individuals along with information on adult health outcomes, bioarchaeology offers another means to approach health from a life course perspective.

2.4 Timing and development

The relevance of stressor timing is embedded in developmental stages of growth; during periods of rapid growth, organs, tissues, and physiological processes are more sensitive to disruption (Ben-Shlomo and Kuh 2002; Lynch and Smith 2005). Therefore, understanding the schedules and growth rates of the different components, and how these interrelate, is useful in considering why infancy and childhood might also include critical or sensitive periods. Changes in brain (weight) and height velocity, along with dental development, are displayed in relation to dietary transitions and

immune development in Figure 2.1. Specifically, this includes development of the mandibular canine, which is undergoing amelogenesis, or enamel formation, and is able to register stress related defects during much of infancy and childhood. Development of the immune system is especially pertinent during early postnatal life, particularly as the infant transitions from a maternally buffered system. Therefore, a brief overview of immune system components relevant to the developmental model is also provided first, including IgG, IgA, and Th1.

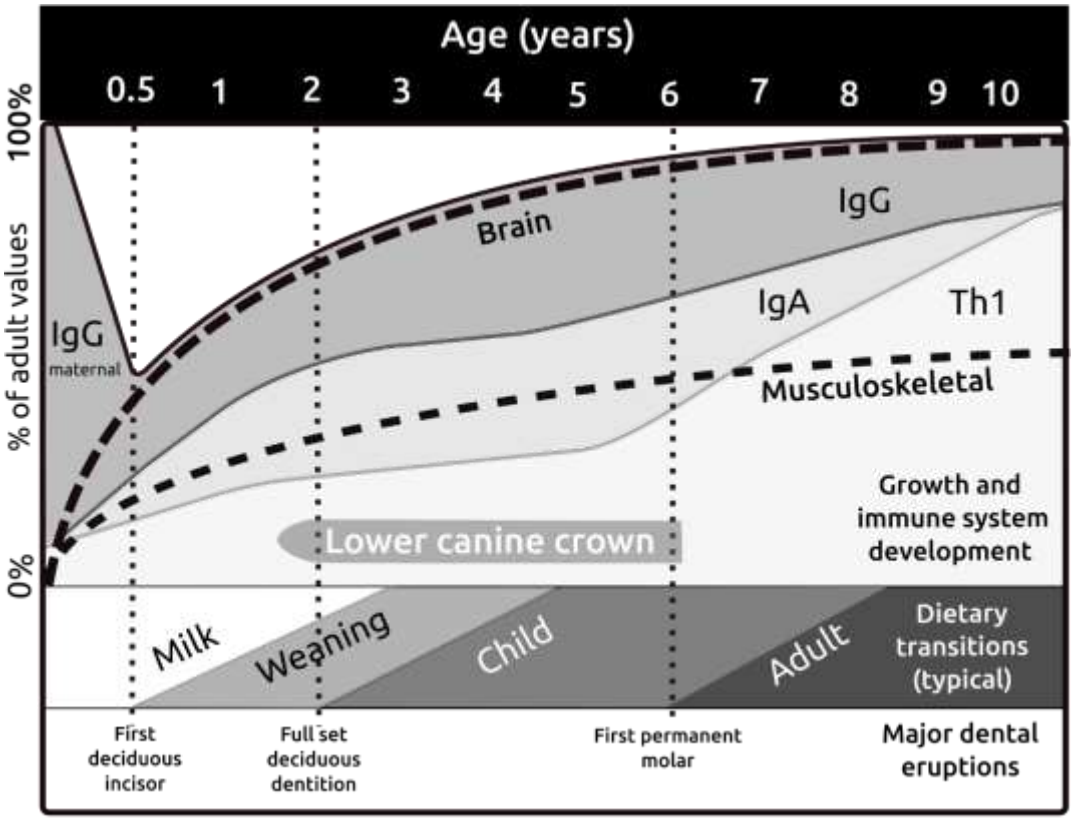

Figure 2.1 Schedule of growth and development from birth to ten years (approximate). Data references: brain and musculoskeletal growth adapted from Paulino et al. 2010; canine crown formation Reid and Dean 2000; dietary transition Bogin 1999; dental eruptions Al Qahtani et al. 2009; Immune function Hannet et al. 1992, Duramad et al. 2007.

2.4.1 The immune system: a basic overview

Defence against infection can be grouped into two main categories: innate and adaptive immunity. Innate immunity included barriers such as skin and mucous membranes as well as cells responsible for releasing protective and signalling biomolecules, such as cytokines, which can regulate both innate and adaptive immune responses (Goenka and Kollmann 2015). Adaptive responses involve cells that 'remember' previously encountered pathogens through recognition of foreign antigens, and stimulates an adaptive immune response, including the production of antibodies. Two types of cells play a major role in adaptive immunity; T and B cells. T cells provide cell mediated immunity in response to antigens, which involves the activation of macrophages and natural killer cells as well as killer T cells and various cytokines (Gregory 2006). In contrast, B cells provide humoural immunity by secreting antibodies, or immunoglobulins, that attach to foreign antigens on the surface of microbes, either neutralizing or marking them for destruction (Gregory 2006).

Two major classes of antibodies, IgG and IgA, provide critical protection for newborn and infants against invading pathogens. IgG is the main immunoglobulin class produced in response to a previously encountered, or remembered, pathogens (Zinkernagel 2001; Gregory 2006; Niewiesk 2014). Importantly, these provide crucial passive maternal protection to newborns, as in addition to being present in colostrum, they are the only class of immunoglobulin able to cross the placental border (Zinkernagel 2001; Gregory 2006; Niewiesk 2014). IgA, on the other hand, is the main immunoglobulin present in breast milk, so it is able to provide passive postnatal protection (Zinkernagel 2001; Gregory 2006; Niewiesk 2014). Thus, the two classes of immunoglobulin perform different roles: maternal IgGs provide protection against

infection via the bloodstream, while IgAs in breast milk mainly protect against pathogens in the gastrointestinal tract (Zinkernagel 2001; Lewis 2008; Niewiesk 2014).

Amongst cell mediated immunity, helper T cells have a major role in assisting and regulating immune responses, primarily through the proliferation of various types of cytokines (Romagnani 1999; Holt and Jones 2000). The cytokines produced by helper T cells form polarised profiles: Th1 and Th2, the ratios of which vary by age and types of pathogen exposure (Holt and Jones 2000). Th1 cells proliferate following intracellular infections by bacteria and some viruses, while Th2 cells proliferate in response to intercellular infestations such as helminths (Romagnani 1999). As Th1 cytokines are associated with intracellular infections, measurements of these proteins at different developmental ages provide a measure of immune development (Romagnani 1999). Serum concentrations of IgG, IgA and cytokines associated with Th1 profiles, assessed at various ages are reported as percentages of normal adult values in Figure 2.1.

2.4.2 Infancy

In general, the first postnatal year of life is characterized by intense but decelerating growth; the brain, in particular (Figure 2.1), grows more rapidly than any other tissue or organ during this stage but gains in body length are also marked. This pattern continues typically into the middle of the third year of life (Bogin 1999). The initial year also sees the transition from a strictly milk diet to the inclusion of supplementary, or weaning, foods, necessary as breast milk alone cannot meet the energy demands of the growing infant after approximately six months (Jelliffe and Jelliffe 1978; Bogin 1999). As the full complement of deciduous teeth are not yet

erupted, supplementary foods need to be soft or easy to masticate and energy rich. Critically, maternal IgG antibodies that protect against intracellular infections wane around six months and reach a nadir prior to the development of the infant's own IgGs through acquired immune responses (McDade and Worthman 1999; Hashira et al. 2000; Zinkernagel 2001; Newburg et al. 2005; Niewiesk 2014; Edwards 2015; Simon et al. 2015*).* Breast milk, however, continues to provide protection in the form of regulatory proteins as well as IgA, which mainly reside in mucosal tissue, such as the gut and respiratory tract, helping to eliminate intestinal and respiratory infections (Zinkernagel 2001; Niewiesk 2014). Their presence, however, is dependent on continued breast feeding (McDade and Worthman 1999). The tension created by the need for supplementary foods due to increasing energy requirements but which heightens the risk of pathogen exposure is known as the weanling's dilemma (Rowland et al. 1978). Of particular concern are food and waterborne enteric pathogens, such as rotavirus and cryptosporidium, which are still major causes of infantile diarrhea and associated mortality (Kotloff et al. 2013; Dennehy 2015). This makes the first year a particularly dangerous period. Not only does the infant require a specialised, diet but the introduction of non-sterile foods exposes them to pathogens at a time when their own immune system is still immature but maternal protection is waning. The impact that variation in weaning practices may have in relation to immune function is discussed in detail below. Weaning progresses until milk is fully replaced by supplementary foods, and although the associated risks gradually become less acute, they still pose a major threat (Duramad et al. 2007).

2.4.3 Infancy-childhood transition

The first few postnatal years represents a further critical time when dental development, dietary transitions, and immunological shifts must again be coordinated to minimise dangers associated with infections but still support growth velocity. Around two years or soon after, all deciduous teeth have erupted, allowing the infant to more easily consume supplementary foods (Figure 2.1). This is commonly when the weaning process is completed (Bogin 1999). At this point, all passive immunity is lost, including immune factors that help regulate the child's still immature response system and help to attenuate infections (McDade and Worthman 1999; Zinkernagel 2001). This represents a critical period in immune development, as in order to acquire their own immunity, they must be exposed to pathogens without passive protection, particularly as maternally acquired antibodies inhibit maturation of their own memory cells (McDade and Worthman 1999; Zinkernagel 2001; Duramad et al. 2007). In addition, although growth velocity has slowed relative to the first year, the brain still demands considerable energy, which peaks around four to five years when it consumes approximately 66% of resting energy expenditure (McDade et al. 2016). Thus, due to restrictions imposed by the deciduous dentition and an immature digestive system (Bogin 1999), early childhood is a period that requires a particularly high quality diet to maintain brain and immune system development at a time when they are still particularly vulnerable to infection and less able to regulate immune responses.

2.4.4 Childhood

The childhood stage follows infancy, from approximately three to six or seven years, on average. Although marked by slower growth velocity compared to previous stages, many children experience a slight growth spurt towards the end of this phase (Bogin 1999). By six years, on average, the permanent first molar erupts, signalling the start of two important developmental transitions (Figure 2.1): completion of brain growth (in weight) and the ability to begin to eat an adult diet (Bogin 1999). By seven years, both of these transitions are usually complete, marking the end of childhood and the beginning of the juvenile stage (Bogin 1999). Although less apparent but just as vital, the child's immune system has also been maturing during this phase, evident by increasing levels of immunoglobulins and helper T cells (particularly Th1, Figure 2.1). Primary exposure to an increasing range of pathogens allows acquired immunity to develop. This means that the immune system can respond to subsequent infections more quickly, but also immune responses are better regulated, resulting in less severe reactions (Gregory 2006; Goenka and Kollmann 2015). This is evident in the markedly decreasing incidence and mortality rates for many infectious diseases towards the end of childhood (Adjuik et al. 2006; Cruz and Starke 2007; Donald et al. 2010).

2.5 Immunity and weaning

A process that can have a major impact on infant and childhood health is weaning, particularly as there are a number of ways that this can exert influence. Weaning represents not only a dietary transition but also a major shift in types of immune defence. During this period, the infant is vulnerable to adverse nutritional and disease exposures at a time when energy demands are still high and immune function is

low (McDade et al. 2016). How long this period of increased susceptibility lasts and how risky it is in terms of mortality is dependent on how weaning is implemented. Early completion, or abrupt weaning, creates a wider window of susceptibility, while a later completion minimises the window. Early and later weaning models are displayed in Figure 2.2, where both hypothetical environments require the same level of immunity, or protection, to minimise mortality risk. Shifting the age when weaning is completed alters the susceptibility gap; the earlier this occurs, the greater the risk of death and the longer the infant remains at risk before their own immune system matures to a level where exposures are less risky. This means that the size of the immunity gap depends on age at initiation and completion of weaning.

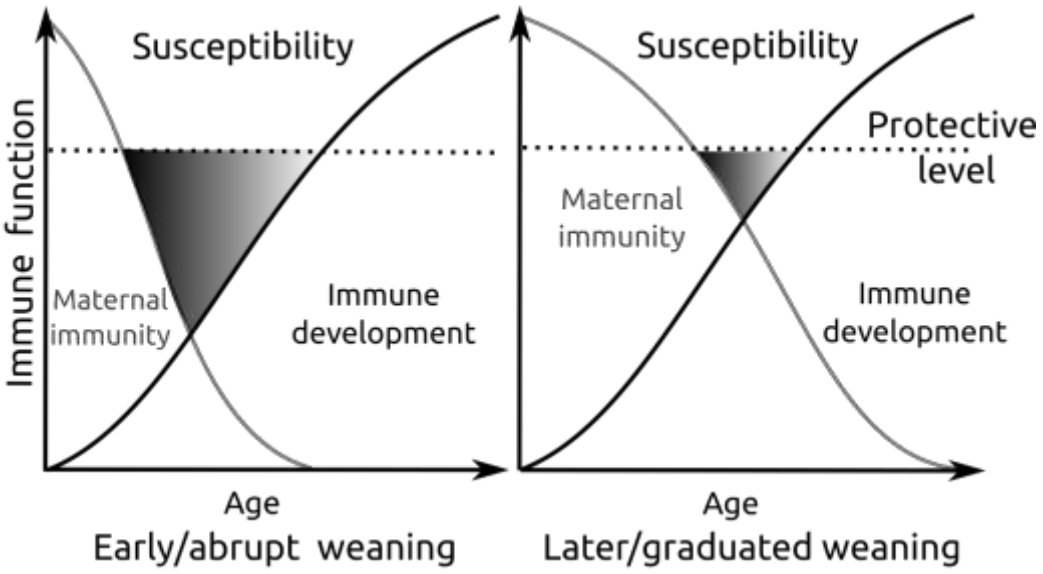

Figure 2.2 Hypothetical models of differential impacts on susceptibility to infection in relation to early and later completion of the weaning process.

Temporally, the weaning process is shaped by age at initiation and the length of time until completion, which can be influenced by a number of intrinsic and external factors. The age when supplementary foods are necessary, due to the infant's energy

requirements, represents the latest that weaning should ideally be initiated (Jelliffe and Jelliffe 1978). The quality of the mother's milk, which can be affected by her health and nutrition status, may prompt early initiation of weaning, as can a subsequent pregnancy (Fildes 1992). Prior to baby formula or refrigeration, if a mother was unable to breast feed the infant due to work demands, for example, the process might be truncated (Fildes 1992). In many premodern European countries, wet nurses were an alternative for those who could afford them, but often these presented a number of problems, including woman attempting to feed a large number of infants in order to earn more money (Fildes 1992). From the Middle Ages until artificial milk formulas were available, it was common practice to shift completely from breast milk to pap or panada, supplementary foods made with bread soaked in cow's milk, water, broth, or beer/wine, often within the first few postnatal months (Hervada and Newman 1992; Obladen 2014). Not only was this nutritionally inadequate, but also a likely source of pathogens. The importance of breast milk over artificial feeding was clearly demonstrated in a study by Knodel and Kintner (1977), who analysed historical data from 19th and 20th century US and German cohorts. The authors showed an inverse relationship between mortality rates and the length of time infants were breast fed. Those who only received artificial feeding had the highest mortality rates, while those who were breast fed the longest had the lowest rates. A marked rise in mortality was evident once breast feeding was concluded (Knodel and Kintner 1977).

The development and functionality of both innate and adaptive immune systems can be hampered by poor nutrition (Marcos, Nova, and Montero 2003; Rytter et al. 2014). This means the susceptibility gap may vary between children of differing socioeconomic conditions to the extent that these influence diet; those in less well-off situations may not only experience increased exposure to pathogens through

overcrowded and unsanitary housing but may also be at increased risk for longer periods, particularly if weaning is truncated. In addition, their ability to respond to infection and recover may also be hindered by an inadequate diet. Therefore, social context may act to not only alter the health risks associated with exposure but also modify subsequent impacts.

Early childhood represents a potentially risky time for exposure to stressors as not only is it a critical period in immune development but energy demands for growth, particularly the brain, are still high (McDade et al. 2016). Furthermore, these risks may be either elevated or alleviated by different weaning practises (Knodel and Kintner 1977; Jelliffe and Jelliffe 1978). Exposure to infections during rapid growth periods places additional demands on energy, which if sufficient, can adversely impact developing organs, including the immune system (McDade and Worthman 1999; Zinkernagel 2001; Prentice et al. 2013). In addition, recovery from physiological damage may be hampered by lack of adequate nutrition (Duramad et al. 2007; Simon et al. 2015), possibly resulting in long term scarring (Preston et al. 1998). Whether an early insult carries a longer term risk may therefore depend not only on the timing of the insult but also on ability to recover. In turn, this may hinge on an individual's ability to avoid subsequent stressors, such as inadequate nutrition and exposure to pathogens. Life course models offer a way to examine how these various stressors might work to affect adult health, including possible pathways connecting them.

2.6 Critical periods and risk accumulation

Life course epidemiology is concerned with biological, behavioural, and psychosocial processes that link adult health to stressors occurring across all stages of

life (Kuh et al. 2004). Operating within this broad timeframe, a series of conceptual life course models have been proposed by Ben-Shlomo and Kuh (2002) that broadly describe different ways in which experiences can influence health (Figure 2.3). These suggest that factors or risks can accumulate over the life course or might be operational only during a critical developmental window of time (Kuh et al. 2004; Lynch and Smith 2005). A critical period model describes a limited window of time when exposure to stressors may impact later health outcomes, but a defining feature is that the specific risk does not exist outside this window (Ben-Shlomo and Kuh 2002; Lynch and Smith 2005). Stressors operating during this period of development may alter the structure or function of organs, tissues, or physiological processes (Kuh et al. 2003; Lynch and Smith 2005). The impact may be unable to be modified by later influences, for example, limb malformations due to uterine exposure to thalidomide between 24 to 34 days post fertilization (Kim and Scialli 2011). In other situations the impact may be modified or worsened by later stressors and it is also possible that an effect is only realised after subsequent stressors act to antagonise the underlying condition (Ben-Shlomo and Kuh 2002). This model aligns with the Barker, or DOHaD, hypothesis and concepts of biological programming (Kuh et al. 2003; Lynch and Smith 2005). For example, exposure to certain infectious pathogens during the first two postnatal years elicits a shift in helper T cell immune responses (the Th1/Th2 profiles), which are associated with a decreased risk of developing atopic diseases; lack of exposure during this critical period is associated with an increased risk (von Hertzen 2000).

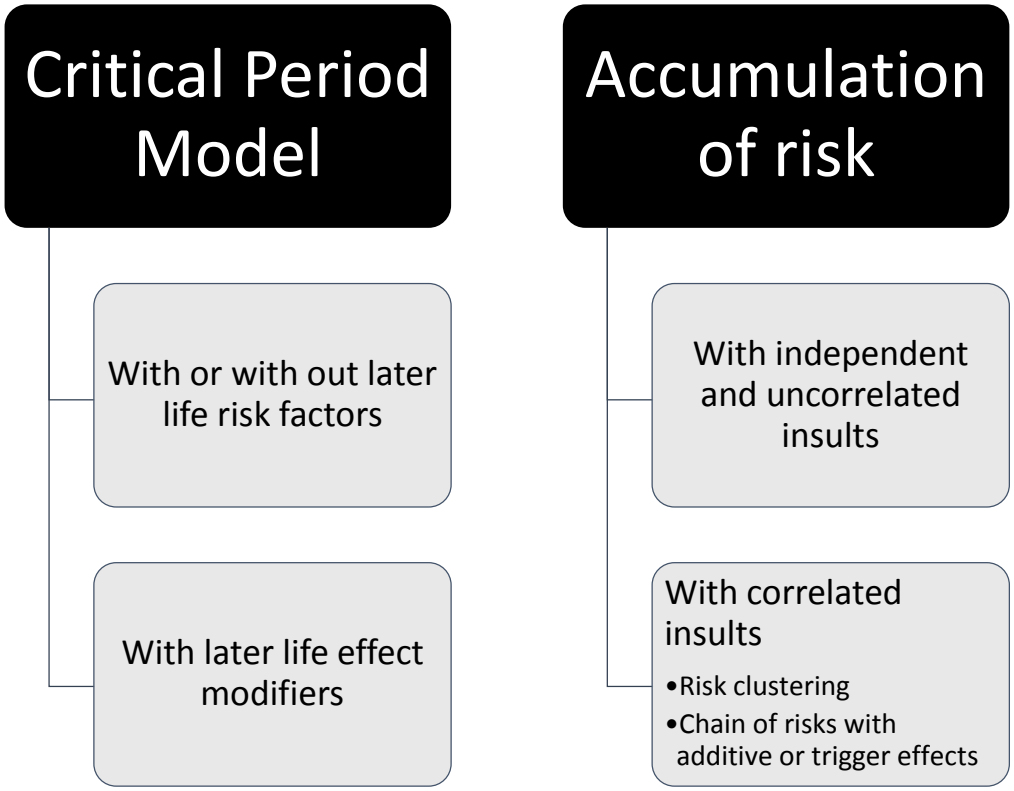

Figure 2.3 Conceptual life course models (based on Ben-Shlomo and Kuh 2002, Table 3) that demonstrate possible ways early and later health can be connected. Variants of the critical period model include situations when subsequent risk factors may reveal initial damage or when initial damage is modified, such as partially reversed, by subsequent influences. Variants of the risk accumulation model can include situations when multiple insults are unrelated to each other. Alternatively the insults may be related to one another through a clustering effect or a cascading chain of risk.

In contrast to a critical period, risk factors may accumulate over time (Figure 2.3). In addition, their impact may also be modified if exposure is during a sensitive period (Ben-Shlomo and Kuh 2002). A sensitive period is when exposures may have stronger impacts than usual but are not limited to a specific time period. These types of impact are more able to be modified later or even reversed (Ben-Shlomo and Kuh 2002). For example, periods of rapid skeletal growth represent sensitive periods when the rate of growth may be more easily impacted by disease or under nutrition. However, if later conditions are suitable, catch up growth can occur and act to minimise, or even reverse, impacts of growth faltering (Prentice et al. 2013). Accumulative risk factors

may be independent of each other, such as experiencing the death of a loved one and experiencing food poisoning. Alternatively, stressors may cluster, such as risky alcohol consumption, smoking, and low education level (Bonevski et al. 2014) or form chains of risk where an initial trigger causes a series of subsequent risks. For example, an unplanned teenage pregnancy may result in a lower education level for the mother, which may increase the risk of lower paid employment and psychosocial stress (Kennedy et al. 2010). The timing of exposure is a relevant aspect to all these models, whether as critical or sensitive periods that can be connected to certain stages of development or their role within a series of escalating risks.

The critical period and accumulation of risk models (Figure 2.3) provide a useful framework to consider how adult health may be influenced by experiences across the life course. They suggest multiple pathways, emphasising how impacts may be time dependent, accumulative, or able to be modified by subsequent experiences. Adverse adult health, for example, might result from a critical period in childhood but only be apparent if there are later modifying affects, or alternatively, could be due to the accumulation of correlated health insults over many years. The models emphasise how health may be the cumulative outcome of various types of stressors, including social and physiological, interplaying and operating at different ages to be viewed as a single dynamic process. Nevertheless, interpreting which pathway might best explain variation in mortality profiles can be difficult if comprehensive information over the life course is not available. Mortality distributions describe variation in the risk of death at different ages, allowing risks between groups of interest to be compared. Considering how these risks might vary at different ages between groups can help elucidate mechanism operating to shape the distributions.

2.7 Scarring and selection

Mechanisms that link early and later life health have been suggested to operate either directly or indirectly on later mortality risks and may exert either negative or positive influences. These mechanisms are particularly useful in understanding how social factors might interplay with early health insults to explain variation in adult mortality risks. Preston et al. (1998) describe a simple two way table of effects (Figure 2.4) that not only allows early and later environments to be linked but in doing so reveals the direction of the relations, which in turn suggests the type of mechanism likely maintaining the relationship. Suggesting specific types of mechanisms narrows the range of possible causes of health outcomes and allows specific questions regarding their nature to be addressed. The mechanisms are treated as discrete in the model, and although in reality they are likely interconnected, they provide a valuable method to consider dominant effects and help to untangle often complex interactions. It is also important to consider that impacts may be negative or positive.

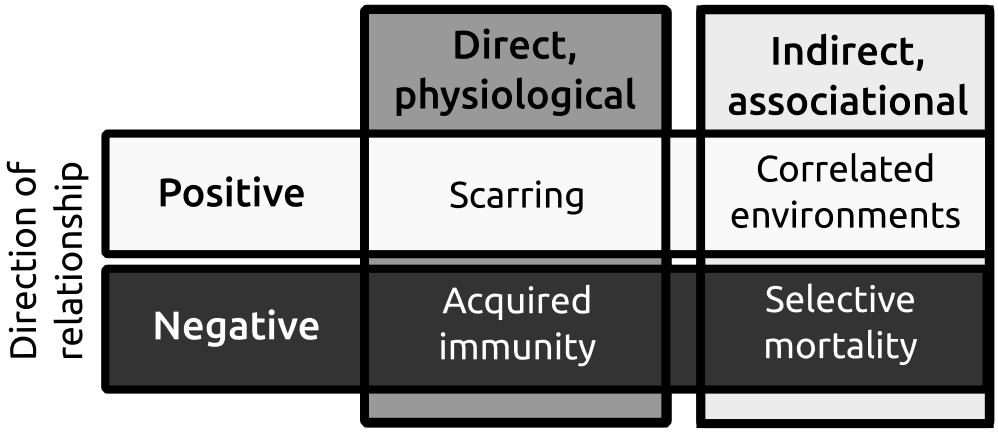

Figure 2.4 Typology of relations between mortality risks in childhood and mortality risks in adulthood (adapted from Preston et al. 1998)

Preston et al. (1998) propose that direct mechanisms are physiological impacts that directly affect the individual's physiology, such as poor nutrition or disease, which may produce either an increased or decreased risk of death in adulthood (Preston et al. 1998). For example, if an increased risk of childhood morbidity is associated with an increased risk of death in adulthood (a positive association), this may suggest that the link results from scarring, or physiological damage (Preston et al. 1998). Alternatively, if a negative correlation is evident, such as when a high childhood risk existed, but is linked to a reduced adult risk, then individuals may have benefited from acquired immunity. Previous exposure to certain antigens, for example, smallpox (variola virus), may offer protection against later exposures.

Indirect relationships describe influences in the individual's environment that operate upon them, such as socioeconomic position, which may act to increase or decrease mortality risks. When early and later mortality risks are indirect and negatively correlated, it may suggest that selection bias is operating (Preston et al. 1998). For example, if mortality was high in childhood but low in adulthood, it may be due to frailer individuals being less likely to survive to adulthood (selective mortality). Conversely, a positive association might suggest correlated environments where high adult mortality was connected to high childhood risks by virtue of the fact that limited access to adequate healthcare or nutrition was a factor in both periods (Preston et al. 1998). What is apparent is that adverse childhood experiences may manifest as either lower or higher adult mortality risks - depending on which mechanism exerts the most influence. This underlines the importance of considering the socioeconomic context of individuals, or groups, when interpreting adult mortality distributions. Identifying which mechanisms are operating between early and later life to elicit either a health deficit or credit means that we can begin to assess likely causes.

Even with insight into socioeconomic environments, it may still be difficult to decipher which mechanisms are operating. In a study assessing survival to at least 85 years in a cohort of African Americans born at the beginning of the 1900s, Preston et al. (1998) found a positive association between adverse childhood environment and earlier death in adulthood. They were unable, however, to determine if the positive association was due to scarring from a direct association, or indirect from correlated environments. They also detected a sex difference in outcomes, which they suggest may point towards an indirect association, suggesting a cultural or social influence rather than physiological scarring (Preston et al. 1998). Conversely, in another life course study using historical data (1766 to1895) for Swedish cohorts with information on social mobility, a high disease load in early life was also positively associated with adult mortality (Bengtsson and Broström 2009). Although a high early disease load also predicted lower wealth accumulation, adult socioeconomic position and mortality were not connected (Bengtsson and Broström 2009). This, the authors suggest, points to direct scarring as a linking mechanism rather than an indirect environmental association. Another consideration is that these mechanisms may not only manifest as polarised states, as both scarring and selection may operate at different times in the same mortality cohort, detectable as mortality crossover.

2.8 Mortality crossover

Mortality crossover results when mortality curves for exposed and unexposed groups cross, often at older ages, but which may only be apparent with certain causes of death (Eberstein et al. 2008). For example, across most adult ages, an exposed group may display decreased survival relative to an unexposed group, but after a certain age,

the two survival curves may converge or actually cross, with the unexposed group then displaying a greater mortality risk relative to the exposed group. Crimmins (2005) suggests that mortality crossover can result from differential mortality selection driven by factors such as socioeconomic status. In this situation, frailer individuals are removed from mortality distributions at younger ages, so after a certain age only the most robust of the originally exposed group remain (Crimmins 2005). A study comparing survival rates of American Europeans and African Americans for a number of adult diseases found that morality curves for influenza/pneumonia and heart related disease in particular, crossed over after 80 years of age, with American Europeans then displaying an increased risk relative to African American (Eberstein et al. 2008). The authors suggest that heterogeneity of frailty may be driving selection but add that early life conditions as well as health differentials in risk behaviours and social mechanisms, including social support or lack of it, shape this heterogeneity (Eberstein et al. 2008).

Heterogeneity of frailty describes how individuals may vary in their susceptibility, or risk, of death, which may arise due to a number of factors including age, socioeconomic position, and previous health experiences (Vaupel et al. 1979; Milner and Boldsen 2017). These causes may be apparent but may also be hidden (Vaupel et al. 1979; Milner and Boldsen 2017), resulting in unexpected shifts in mortality rates between groups. Heterogeneity of frailty was suggested to explain results in an analysis of prisoners who survived the American Civil War (Costa 2012). The author found men who were under 30 years at the time of imprisonment experienced higher mortality and morbidity rates in old age than men who were older at imprisonment, while men over thirty experienced higher mortality rates during imprisonment (54% compared to 30%). This suggested that selection dominated their

mortality rates in old age (Costa 2012). The heterogeneous risk of death in old age was explained by age at incarceration (Costa 2012).

Mortality crossover has also been observed at younger adult ages, suggesting that in some environments, the effects of selection and scarring may operate earlier, but also the age when crossover occurs may vary considerably by sex. A recent study using Swedish data considered mortality curves across the life course in conjunction with detailed information on early stressor timing (Quaranta 2014). The author found cohorts exposed to high disease load in early life had decreased life expectancy for the first post natal year, but variation in survival curves differed markedly by sex over the life course. For females, those exposed show decreased mortality from infancy until their mid-forties relative to the unexposed females, after which the mortality risk for exposed exceeded the unexposed (Quaranta 2014). Exposed males, on the other hand, had a lower mortality risk until age 19, relative to unexposed males, after which the risks for exposed males exceeded the unexposed. After fifty years of age the risks of death were similar for the two male groups (Quaranta 2014). The author suggests that mortality crossover for females is due to selection dominating the exposed group until their forties, after which scarring caused a relative increase in mortality risk. Selection dominated exposed males until their late teens, after which scarring operated to increase their risk (Quaranta 2014). The negative impact of early stressors appears to have operated on males across most of adulthood, while for females it was only detectable in older adulthood. As mechanisms that shape mortality distributions, selection and scarring are interlinked with the notion of frailty. Selection results when frailer individuals are lost earlier in the mortality schedule, leaving more robust individuals to survive to older ages. It is analogous with a culling effect. Scarring, on the other hand, is when individuals who may not have been previously frail survive longer but become

frail at a later age, such as when latent affects are exacerbated by declining immune function in old age (Gregory 2006; Simon et al. 2015).

2.9 Frailty and the skeletal record

In demography, the term frailty refers to an individual's risk of dying relative to others in their cohort (Vaupel et al. 1979). The frailer an individual is, the more likely they are to die. In public health studies, frailty describes the consequences associated with loss of function or disability, but which may also link to variation in mortality risks (Verbrugge 2005). In bioarchaeology, we start from the end result, death, and work backwards, which means mortality profiles are used to try and understand how the risk of death may have varied in the living. For example, by considering those who died at a younger age, bioarchaeologists attempt to identify commonalities that might define them as a group, which might be factors such as levels of disease exposure or access to resources, thereby identifying factors that influenced frailty in the living. One issue, in both the living and the dead, is hidden heterogeneity – where frailty may vary among individuals or groups due to unknown reasons (Wood et al. 1992). This is a particular problem when only aggregate data are analysed as variation in the risk of death between subgroups cannot be considered (Wood et al. 1992). Although hidden heterogeneity will always be present to an unknown degree, much can be resolved by considering commonalities shared by individuals that may have placed them at greater risk of dying.

Researchers have suggested that some skeletal lesions, such as active periosteal new bone formation, are useful indicators of frailty because they have been linked with a younger age at death (DeWitte 2014). Thus, in bioarchaeology, the concept of frailty is inextricably linked with the concept of selection, or selective mortality, which

describes death as biased towards frailer individuals (Wood et al. 1992). This means that the frequency of skeletal lesions associated with frailty cannot be used to directly infer frailty in the living population, as those who died possibly represented a distinct subgroup within the living population. In cemetery collections, skeletal lesions associated with decreased survival will always occur at higher frequencies in the dead compared to living groups (Waldron 2009). In some situations, lesions, such as those associated with periodontitis, are not so much associated with an increased risk of death but rather with age (Wasterlain et al. 2011). As severe periodontitis has been associated with chronic morbidities in the living (e.g. Nelson et al. 1990; Garcia et al. 2001; Scannapieco et al. 2003), in such situations they might offer subtle insight into chronic adverse health experienced well prior to death. How they are interpreted will depend on their association with death for each group in question.

A further issue with selective mortality is how the pressure it exerts on the living shifts with mortality rates (Wood et al. 1992). During periods of low mortality, death is more selective towards the frail but during periods of high mortality, such as crisis mortality, it becomes less selective. This means, for example, in attritional cemeteries (cemeteries resulting from normal population attrition), a greater percentage of skeletons may have indicators of frailty compared to those from a catastrophe cemetery. This situation is evident in a study by DeWitte and Wood (2008), where they found that mortality was less selective towards individuals with stress lesions (associated with frailty) in a Black Death catastrophe cemetery than in an attritional cemetery where generally lower mortality rates would be expected. Although some degree of selection may still occur even in times of extremely high mortality, it will probably be markedly less than in low mortality periods. This has implications when comparing skeletal lesions between groups, because if they experienced different mortality pressures, then

their lesion frequencies may not be directly comparable. What is unclear is the potential impact that differential mortality rates may have between less extreme groups. More specifically, at what point might differences in mortality rates exert differential selective pressures that make comparisons of lesion frequencies meaningless and how similar do they need to be before comparisons are meaningful?

As pointed out by Wood et al. (1992), a skeletal collection with fewer stress indicators does not necessarily imply that the living population was in better health than those represented by a skeletal group with more stress indicators. Further paradoxical issues with skeletal analyses arise because of the time it takes for disease processes to form bony lesions. This means that stress indicators are only present in the skeletons of individuals who survived the stressor long enough for lesions to form; those that succumbed quickly are unlikely to have formed lesions (Ortner 2003; Wood et al. 1992). Therefore, stress indicators can be interpreted as a sign of survivorship as well as frailty (Goodman 1993). As they are not mutually exclusive states, their interpretation needs to consider the wider group context including the overall crude prevalence of lesions (For example, are the lesions ubiquitous?), the age distribution (Are they more concentrated in the young?), and social structuring (Are high and low socioeconomic groups equally likely to have the lesions?). Understanding how stress indicators are generally distributed as well as how they vary amongst groups and in terms of age at death can help establish when stress indicators are a sign of survival or frailty.

2.10 Conclusion and application to current research

A life course approach points to the existence of vulnerable developmental periods, when stressors may impose a particular deleterious outcome but which may be

modified, both positively and negatively, by environment conditions working across the life course. Although insult timing is understood to be a relevant factor in later outcomes, particularly during foetal and the first year of postnatal life, less is known about vulnerable periods during childhood. The significance of stressor timing is connected to variations in the developmental pace and schedules of maturing organs, tissues, and processes, which are particularly susceptible to interruption during periods of rapid growth. Interplay between immune and dietary transitions, such as weaning and maturation of acquired immunity, can create a vulnerable period where individuals have a heighten susceptibility to disease. As immune development is a lengthy process, this window of susceptibility can extend well into childhood.

Conceptual life course models explain ways that early insults may link to later health. In addition, risks – especially those related to socioeconomic environments, can accumulate across the life course to also culminate in later adverse health. This emphasises the need to consider the socioeconomic environment when attempting to identify putative causes relating to adverse adult health. Differential socioeconomic environments can also complicate how adverse health outcomes may shape mortality profiles. Mechanisms such as scarring and selection can both operate to create apparently similar mortality risks in adulthood, but which may originate from different causes. Shifts in mortally risks between groups, such as mortality crossover, however, can provide insight into which mechanisms may have been operating on groups at different ages. These mechanisms reflect heterogeneity in frailty, indicators of which, along with an understanding of the socioeconomic environments, can help untangle sometimes paradoxical outcomes in mortality schedules.

Childhood presents a window of vulnerability that can influence later health, but before possible impacts can be identified, one needs to consider how they might appear

in the skeletal record. In this research, I aim to investigate whether later health outcomes might result from stressors operating during childhood but also how these outcomes might influence and be influenced by subsequent risks. I will also consider the different pathways, such as the critical period or risk accumulation models, which might connect early and later health, including how these might appear in the skeletal record. Skeletal data, along with socioeconomic information, should help establish the direction of the relationships connecting early and later life environments and focus on likely causes underpinning the association.

Skeletal and dental indicators of subadult stress used in this research that might relate to adult mortality and morbidity are presented in Figure 2.5. These have been divided into direct and indirect to reflect Preston et al.'s (1998) terminology, with indirect group influences able to operate across the life course. Direct subadult factors include indicators of early physiological insults that may still be evident in adult skeletal remains, including enamel hypoplasia, porotic lesions (cribra orbitalia and porotic hyperostosis), and variation in femoral and tibial lengths. The ages when these insults are most likely to cause lesions or impose skeletal alterations tend to vary and are discussed in more detail in chapter four. Direct adult factors may be apparent either as increased or decreased risk of earlier death, periodontitis, or occurrences of periosteal new bone formation. These potential subadult impacts and adult outcomes, however, cannot be assumed as direct cause and effects, since indirect influences can produce outcomes that appear contradictory, if taken at face value (Wood et al. 1992). Therefore, how group influences might shape frequencies of direct insults needs to be considered.

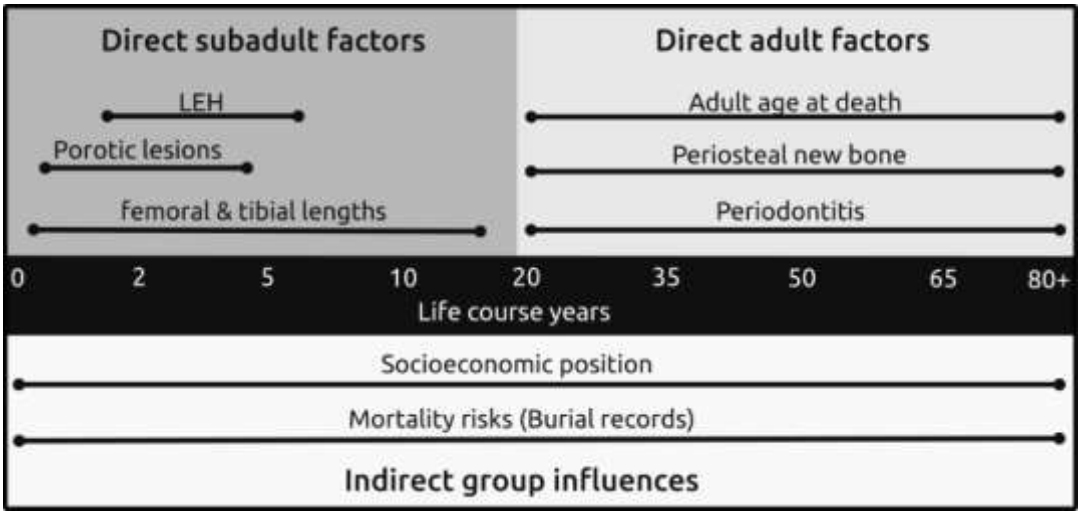

Figure 2.5 Factors and influences operating over the life course used in this study. LEH = linear enamel hypoplasia. Porotic lesions include cribra orbitalia and porotic hyperostosis.

Indirect group influences can include socioeconomic position operating across an individual's entire life course. This is considered an indirect group effect because it does not directly operate on an individual's physiology, such as infection or under nutrition, but depending on the socioeconomic group affiliation, shifts the likelihood that an individual will be exposed to stressors as well as the subsequent implications of exposure (Preston et al. 1998). Mortality risks are also an indirect group influence operating across all ages, which in this research are obtained from parish burial records that relate to higher and lower socioeconomic groups. Variation in mortality risks represent differential force of mortality exerted on the living, with the frailest in any age group at greatest risk of death (Wood et al. 1992; Preston et al. 1998). Assessing these risks over the life course can help determine whether selection or scarring mechanisms might have impacted adult mortality profiles. Understanding how socioeconomic position and mortality risks across the life course may shape mortality distributions should help identify if direct or indirect mechanisms are operating in adulthood that may reflect health insult experienced in childhood.

CHAPTER THREE: DENTAL AND SKELETAL INDICATORS OF STRESS

3.1 Introduction

Recently the relevance and importance of employing a life course approach in bioarchaeology has been convincingly outlined (Agarwal 2016). In addition, the value that bioarchaeology can bring to life course epidemiology should not be underestimated. Nonetheless, before lifelong associations between early stressors and later adverse health markers in skeletal remains are examined, their benefits and limitations should be carefully considered. This chapter outlines and discusses the nature of various stress skeletal and dental indicators used in this research. The first section deals with indicators reflecting direct physiological health insults associated with infancy and childhood. Often the earliest skeletal indicators are cribra orbitalia and porotic hyperostosis, frequently connected to types of anaemia experienced during subadult development (Stuart-Macadam 1985; Walker et al. 2009; Oxenham and Cavill 2010). Studies that have analysed the timing of active cribra orbitalia and porotic hyperostosis in subadults who lived in industrialised London suggest they most likely reflect stressors operating in infancy and early childhood, specifically between six months and two years (Lewis 1999:177). Therefore, as these lesions might reflect the earliest stressors recorded in this research, they are discussed and analysed first. Enamel hypoplasias are particularly useful as they allow the age of the individual when they experienced stressors to be estimated (Goodman and Rose 1990; Hillson 1996). As hypoplastic defects are the main focus of analysis in this research, studies that have investigated their relationship with survival are discussed at length. Femoral and tibial

lengths can provide evidence of chronic growth faltering (Steckel 1995), which may have been influential over a wider age range including adolescence so these are considered last in the series. These early stress indicators are used to assess how developmental environments may have varied for children of differing socioeconomic groups living in London during the Industrial Revolution.

Following on from childhood, direct physiological indicators reflecting adult health risks are discussed. Adult mortality is the definitive stress indicator and is assessed using age at death estimations. A Bayesian approach is used to assign age at death and is discussed further in chapter four. Some forms of skeletal lesions can provide insight into certain chronic conditions and inflammation experienced prior to death. These, in turn, may provide insight into an individual's general health status. Specifically, an overview is provided for periodontitis, which results from oral bacterial infections (Li et al. 2000), and periosteal new bone formation, which occurs in response to inflammation effecting the periosteum (Weston 2012). Again, these are considered in relation to the frequency and timing of hypoplastic defects to determine if associations might be present, as well as how they might vary by socioeconomic group.

Socioeconomic status is used to assess indirect, or associational, group influences. This operates across the life course, impacting direct physiological factors of both subadults and adults. Information on the socioeconomic positions of the samples used in this research is derived from historical and archaeological sources, discussed in chapter four. Indirect group effects include mortality risks, which are established from mortality profiles. As age at death of the skeletal samples may not accurately reflect the actual risks experienced by the socioeconomic groups, due to the skeletal sample selection criteria, information is obtained for the highest and lowest

social groups using burial records for the parish of St. Brides. Collection of these data is also explained in chapter four.

3.2 Childhood stress indicators

3.2.1 Cribra orbitalia and porotic hyperostosis

Porotic hyperostosis and cribra orbitalia describe lesions on the cranial vault (frontal, parietals, and occipital) and orbital roofs (cribra orbitalia) that occur as a result of diploic expansion due to marrow hypertrophy (Stuart-Macadam 1985; Ortner 2003; Rivera & Lahr 2017). The lesions, which may be pitted or porous in appearance and may involve raised areas of trabecular outgrowth (Stuart-Macadam 1985), are commonly reported in bioarchaeology investigations and are used to provide insight into diet and disease. Previously, porotic hyperostosis and cribra orbitalia were assumed to both describe the same underlying process of diploic expansion, varying only in the location of the lesions. Recently, however, research using micro computed tomography scans found individuals with cribra orbitalia had significantly thinner diploic bone and thicker outer and inner tables suggesting the two types of lesion may reflect different aetiologies (Rivera & Lahr 2017). Although, in bioarchaeology, both types of lesions are frequently referred to collectively as porotic hyperostosis, here both terms are used to differentiate between them, as their varying distributions are briefly discussed.

In bioarchaeology, active lesions are most frequently reported in crania of infants and children, but rarely in adults, suggesting that in adults they are mostly residual and indicative of anaemia experienced in the first five or so years of life (Stuart-Macadam 1985; Mittler and van Gerven 1994; Lewis 1999; Walker et al. 2009). However, in some cases active lesions are reported in adults, particularly females or

individuals of lower status (Sullivan 2005). Hereditary anaemias, such as beta thalassemia or sickle cell anaemia, chronic marrow hyperactivity may also persist into adulthood (Stuart-Macadam 1985; Schultz 2001). In general, cribra orbitalia is more frequently recorded than porotic hyperostosis in adolescence and adults, with active outgrowths of trabecular structures primarily limited to infants and children (Stuart-Macadam 1985; Schultz 2001). The reason why lesions are more common in infants and children is thought to be due to age related changes in marrow composition. From birth, all marrow cavities hold hematopoietic (blood producing) marrow, which is gradually replaced at many sites by non-hematopoietic fatty yellow marrow (Tavassoli 1989). By around four years the replacement of yellow marrow is advanced and by adolescence largely complete, with red marrow sites in adulthood contained to long bone epiphyses, cranium, vertebrae, ribs, and pelvis (Ascenzi 1976). This means that in adults, if increased production of red blood cells (RBC) becomes necessary, yellow marrow can be converted to red (Ascenzi 1976). In young children, however, all sites already contain red marrow, so increased production of erythrocytes is more likely to occur via red marrow hypertrophy. This causes an expansion of diploic bone beyond its normal limits. The result is expansion of the diploe and destruction (osteolysis) of the cortical bone – evident as porosity on the bone surface, with orbital roofs and vault regions particular vulnerable. Evidence from radiographs and skeletal remains suggest that incidences of diploic expansion are most likely to occur between six months and five years of age, with active lesions unlikely after twelve years (Stuart-Macadam 1985; Mittler and van Gerven 1994)

In bioarchaeology, porotic hyperostosis and cribra orbitalia are often considered evidence of iron deficiency anaemia. As iron is a key constituent of haemoglobin (the oxygen carrying protein in RBC) its deficiency is a common cause of anaemia leading

to the characteristic diploe expansion (Oxenham and Cavill 2010). However, some researchers have argued that iron deficiency will actually inhibit bone formation and diploe expansion, as iron is necessary for marrow hypertrophy and point to other micro deficiencies as likely causes (Walker et al. 2009). Megaloblastic and haemolytic anaemias are suggested as likely causes of the cranial lesions, as these cause either underproduction, loss, or ineffective RBC, resulting from a combination of poor diet and high disease exposure (Walker et al. 2009), but also some chronic disease conditions (Oxenham and Cavill 2010). With haemolytic anaemia there is abnormal destruction or defective production of RBC, as in thalassemia and sickle cell disease, but this condition can also occur in response to infections, particularly *M. pneumonia* in children (Elebute and Kesse-Adu 2015). Megaloblastic anaemia is due to impaired DNA synthesis that causes RBC to grow rather than divide and is most commonly attributed to vitamin B_{12} deficiency (Hoffbrand et al. 2012). Pernicious anaemia, a megaloblastic form, can result from malabsorption of vitamin B_{12} in the small intestine due to diarrheal disease, parasitic infections, as well as a diets lacking the vitamin (Stabler and Allen 2004). This means groups with low dietary consumption of meat and animal products are particularly at risk, as are infants who are breast fed by mothers with low levels of B_{12}. (Stabler and Allen 2004).

Importantly, recent molecular research has identified a significant relationship between the presence of cribrotic lesions, decreased iron levels, and lower δ^{15}N isotope values, suggesting the consumption of lower trophic levels foods (Zariſa et al. 2016). While this study confirms a relationship between cribrotic lesions and diet, the authors warn that the decreased iron levels could also reflect vitamin B deficiencies (Zariſa et al. 2016). To further complicate interpretations of cribra orbitalia and porotic hyperostosis, some researchers have pointed out that deficiencies of both iron and

vitamin B_{12} commonly co-occur in individuals (McIlvaine 2015). This could mean that a deficiency in $B_{12,}$ by inhibiting marrow hypertrophy, might mask skeletal evidence of iron deficiencies i.e. diploe expansion. The authors warn that a lack of porotic hyperostosis does not necessarily mean that the individual did not suffer from low iron levels (McIlvaine 2015).

It has been suggested that orbital lesions associated with scurvy (vitamin C deficiency) and rickets (vitamin D deficiency) may be mistaken for cribra orbitalia, as these too can cause porosity in the orbital roofs (Ortner and Mays 1998; Steyn et al. 2016). Although the two conditions frequently co-occur, they can be identified by additional information including the patterning of lesions such as sphenoid porosity in the case of scurvy (Ortner and Ericksen 1997; Brickley and Ives 2006) and flared metaphyses and bone curvature in rickets (Ortner and Mays 1998). As I am analysing adult skeletal remains, it is likely I will mainly encounter residual porotic lesions in the orbits. Without the aid of histological or radiographs, it may not be possible to determine if the residual lesions originated in response to diploic expansion or to chronic bleeds in the superior wall of the orbits, such as with scurvy (Ortner 2003). However, such lesions still provide useful information about the developmental environments experienced by differing socioeconomic groups and point towards variable levels of exposure to disease and poor nutrition during infancy and childhood. So although contention may surround whether porotic lesions are mostly due to iron or vitamin B deficiencies as well as when orbital lesions might reflect other micro nutrient deficits, it is clear that the lesions are all associated with adverse development conditions where both pathogen loads and poor diet are likely to be key. For these reasons, porotic hyperostosis and cribra orbitalia are interpreted more generally in this research as indicators of micro-nutrient deficiencies.

3.2.2 Enamel hypoplasia

Enamel hypoplastic defects are particularly useful nonspecific stress indicators visible in tooth enamel. In the permanent dentition, these developmental defects are records of disturbances in enamel matrix deposition, frequently in response to physiological stressors in infancy and childhood (Goodman and Rose 1990; Hillson 1996). This section will begin with a brief overview of hypoplasia defects before discussing how research has unfolded to substantiate enamel hypoplasia as a reliable gauge of physiological stress. However, research findings that appear contradictory to general trends are also discussed, such as when their occurrences in a population are not associated with decreased age at death. This section concludes with a review of the few studies that have used hypoplastic defects and age at death to explore explanatory models linking early stressors to adverse adult outcomes.

Enamel hypoplasia can present in several forms, including pit, plane or linear types. In bioarchaeology, linear enamel hypoplasia is the most commonly recorded hypoplasia, which appears as horizontal grooves in the enamel surface, usually more pronounced on the buccal or labial surface (Hillson 1996). These result when a band of ameloblasts prematurely cease enamel matrix production before producing the full thickness of enamel (Hillson and Bond 1997; Witzel et al. 2008). Pit type defects are less commonly noted and may present as a single circular cavity, a line of multiple pits, or a scatter of pits over a wider area (Hillson 1996). Plane defects are the least common, appearing as broad or irregular areas of missing enamel often with a marked cervical ledge. Sometimes they reveal an irregular area of exposed striae of Retzius, marked with Tomes process pits (Hillson 1996; Witzel et al. 2008).

Hypoplastic defects can occur in response to systemic insults, trauma to the forming crown, or due to genetic conditions such as *amelogenesis imperfecta* (Hillson 1996; Brook and Smith 1998). If caused by systemic perturbations, the same insult will register in lateral enamel as a linear groove on all teeth forming at that time, although the prominence may vary depending on the tooth and position thereon (Hillson and Bond 1997). Defects due to trauma can be identified as localised areas of defective enamel, where either the secretory ameloblasts or newly secreted enamel matrix (which is soft and largely unmineralised) has been damaged (Suckling 1980). This can occur when a deciduous tooth is knocked causing its roots to damage the forming permanent crown or if the overlying deciduous tooth becomes infected (known as Turner's hypoplasia), the inflammation may interrupt normal amelogenesis (Suckling 1980). This type of defect will tend to be localised and only on the affected tooth. It is also less likely to present as a linear defect as direct damage to secretary ameloblasts tends to result in irregular plane type defects, as Suckling (1980) demonstrated using a sheep model. Why some lesions appear as pits is not well understood, but research suggests these might be evidence of more severe stress responses where cohorts of cells have not been able to continue amelogenesis after the stress episode (Witzel et al. 2008). Plane type defects also appear to be caused by severe episodes where a large contingence of cells are permanently interrupted (Witzel et al. 2008). Genetic conditions tend to be rare in most populations and also defects tend to implicate more of the dentition, including discolouration and highly disturbed or missing enamel (Hillson 1996; Brook and Smith 1998; Seow 2014).

In summary, enamel defects that result from systemic stress episodes can be differentiated from those caused by trauma or of genetic origin by their appearance and patterning across the dentition. Linear defects reflect the occurrence of a systemic stress

response, evidenced by all ameloblasts at a certain secretory stage being affected and producing a line of defective enamel. The systemic nature of the cellular response is also evident in that all crowns undergoing secretory stage amelogenesis will register disturbed enamel. Tracking these defects across multiple teeth is referred to as chrono-matching. Defect prominence, however, may vary by location within a crown as well as across tooth types - some may only be detectable histologically (Hillson and Bond 1997). Linear defects can be differentiated from ones of traumatic origin as the latter are only on teeth subjected to trauma so cannot be chrono-matched but also tend to present as localised and irregular areas of defective enamel. Genetic defects usually result in obvious generalised enamel deficiencies, such as thin or discoloured enamel with multiple irregular plane type defects affecting most of the dentition (Brook and Smith 1998; Seow 2014).

Enamel hypoplasia was first clearly associated with disease in the 19th century when Hutchinson (1861) suggested their use in diagnosing congenital syphilis. They were later described by Zsigmondy (1893), who first referred to them as enamel hypoplastic defects. Later, experimental animal studies helped to demonstrate a causal relationship between the defects and induced stress, specifically nutritional deficits (Mellanby 1918, 1927; Klein 1931). Schour (1936) first described the neonatal line, a dark band present within the enamel of most deciduous teeth, as being associated with birth. This line was later associated with external hypoplastic defects in children who had suffered birth defects (Kronfeld and Schour 1939). The relationship was further substantiated when histological analysis identified defective enamel, still in the process of forming, along with associated damaged cells in the developing teeth of stillborn neonates (Kreshover 1940). A study by Sarnat and Schour (1941) attempted to directly relate the occurrence and timing of defects with known age of illness, based on medical

records, of 60 individuals. Despite assuming that the pace of crown formation is constant and that defect width provides direct information on illness duration, assumptions now known to be incorrect, Sarnat and Schour (1941) were still able to associate just under 50% of the known health insults from systemic and infectious disease with enamel defects. While this study was able to relate many episodes of illness with defect occurrence, it led to the realisation that illness does not always result in a defect and conversely defects did not always have a known cause, at least which could be related to a doctor's visit. Sarnat and Schour (1941) also limited their study to ten specific systemic and infectious diseases (measles, chickenpox, convulsions, diarrhea, pneumonia, scarlet fever, diphtheria, vomiting, whooping cough, and rickets). This suggested that there may not always be a direct link between specific diseases and the occurrence of hypoplastic defects, pointing to the existence of additional factors influencing their development.

A series of important controlled animal experiments were undertaken in the 1980s that demonstrated how enamel formation was disrupted at a histological level due to trauma and physiological stress (Suckling 1979; Suckling 1980; Suckling et al. 1983; Suckling and Thurley 1984). Of particular interest was one in which lambs were administered various parasite loads to induce a range of systemic stress responses. The lambs were then monitored until death, after which their teeth were analysed (Suckling et al. 1983). This was significant because the research design allowed for causation to be established, as well as an assessment of the dose response between the degree of systemic stress and defect development. The lambs that were administered large doses of a particularly pathogenic parasite experienced severe and acute (7-10 days) diarrhoea and weight loss. All in this group had hypoplastic defects (Suckling et al. 1983: 397). The enamel in lambs that received lower doses of less pathogenic parasites experienced

milder, but prolonged symptoms (for example, slight diarrhoea for ~54 days). Defects in these animals did not differ to the controls unexposed to parasites. The study demonstrated that hypoplastic defects visible on the crown surface were only associated with acute and severe systemic disturbances, but not chronic conditions.

It is of interest to note that in recent work analysing hypoplastic defects in children who experienced the Irish Potato Famine between 1845–1852, relatively fewer defects were found to have formed during the worst years of the famine (Geber 2014). The author also notes that children with previous defects survived for at least two years longer, on average, than children without defects, possibly reflecting that previous exposure to infection lowered the risk of death during the famine. Geber (2014) explains this by pointing out that during famine periods, most people actually succumb to infection before actual starvation, as suggested by Mokyr and Gráda (2002) in their detailed assessment of causes of death during the Irish famine. Correlation, rather than causation, may also explain higher incidences of defects reported by some researchers who examined nutritionally stressed individuals, such as survivors of the Chinese 'Great Leap Forward' famine (Zhou and Corruccini 1998) and protein supplementation programmes in Mexico (Goodman et al. 1991) and Guatemala (May et al. 1993). However, not all reported this pattern. For example, Infante and Gillespie (1974) found that frequencies of enamel hypoplasia in Guatemalan children did not vary between children who received protein supplementation, or had benefited in utero from their mother's receiving supplements, compared to children who did not receive supplements. However, the authors note that occurrences of hypoplastic defects did reflect annual seasons, where highest frequencies coincided with months that had the worst incidences of diarrhoeal disease (Infante and Gillespie 1974). Goodman et al. (1991) found Mexican infants and children who received daily nutritional supplements

had lower frequencies of enamel hypoplasia, but also fewer episodes of illness. The author's considered respiratory and gastrointestinal infections to be an immediate cause of enamel hypoplasia in this study (Goodman et al. 1991:780). Information on morbidity and hypoplasia was also collected on Guatemalan children up to three years of age who had received nutritional supplementation and compared to children who had not (May et al. 1993). The authors reported that in addition to increased frequencies of hypoplasia in children who received less supplementation, they were reported ill for a greater percentage of time (May et al. 1993:40).

In a more recent clinical dentistry study of modern British families, an aetiological survey was undertaken to help identify factors which might contribute to dental defects (Brook and Smith 1998). The purpose of the study was to provide dentists with information they could pass on to patients who might query the cause of defects, specifically as there were a number of medicolegal cases where plaintiffs claimed their defects were related to excessive fluoride ingestion (Brook and Smith 1998:151). For this reason, the focus was on general classes of causal explanations rather than identifying specific agents. The authors found all linear defects on anterior teeth could be attributed to episodes of systemic illness prior to three years of age. They also noted that in most cases this was due to infectious diseases. Furthermore, seven out of 18 defects on first molars, all of which occurred in the occlusal third, were associated with infection at an early age (Brook and Smith 1998:154). While the remaining defects could not be retrospectively associated with any specific cause, low birth weight and birth trauma were able to be excluded as possible agents.

These studies may suggest that hypoplastic defects are more reflective of acute systemic interruptions, such as occurs with many infectious diseases, rather than more chronic conditions, including severe under nutrition. It is possible that as a stress

indicator, enamel hypoplasia informs more on exposure to infection, while indirectly reflects nutrition. It is also apparent, however, that the underlying aetiology of enamel hypoplasia is not due to one specific cause or infection, rather they are an indicator that physiological stressors were sufficient to a cause systemic interruptions to enamel matrix deposition (Goodman and Rose 1990). This is why they are particularly useful: potential causes of physiological stressors are numerous and individual responses to these stressors are highly complex and variable, but the occurrence of a hypoplastic defect is a clear indication that an individual experienced a systemic response to a stressor sufficient to interrupt amelogenesis.

In their seminal paper on enamel hypoplasia, Goodman and Rose (1990) first suggested a threshold model to conceptualise the relationship between defect occurrence and physiological stress. Their model (Figure 3.1) describes how variation in nutritional status may alter the threshold at which a defect might result from illness (Goodman and Rose 1990:74). The model also relates this threshold to disruption of the enamel forming cells, ameloblasts, which are responsible for the physical manifestation of the defect, thereby suggesting a relationship between defect expression and the degree to which the threshold has been exceeded. This model helps to explain why not all stress episodes result in hypoplastic defects as well as highlighting the synergistic relationship between disease and nutrition in breaching this threshold.

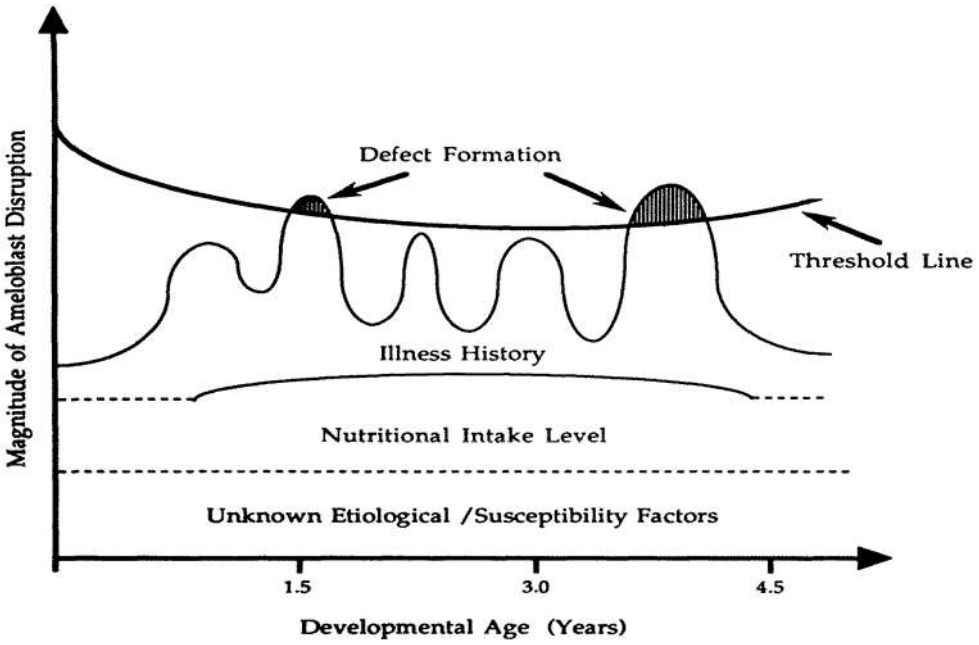

Figure 3.1 Threshold model for hypoplastic defect formation proposed by Goodman and Rose (1990:75)

Inadequate nutrition and infectious disease tend to go hand in hand, but there are several ways these interplay. Poor nutritional status, such as protein-calorie malnutrition, can directly hamper immune responses, particularly cell mediated immunity (Chandra 1991; Rodríguez et al. 2011; Scrimshaw and San Giovanni 1997). This makes undernourished individuals especially vulnerable to opportunistic pathogens, for example underweight children are at greater risk of diarrhoeal diseases (Chandra 1991; Rodríguez et al. 2011). Impaired immunocompetence not only means these individuals are at greater risk of contracting infectious diseases, but will have fewer energy resources available for defence mechanisms. Febrile response, or fever, is particularly expensive to maintain and can result in the catabolism of contractile muscle protein in order to free amino acids for conversions to glucose, which is effectively fuel for maintaining the fever (Beisel 1995). The accumulative effect of increased energy demands and the catabolic shift to adipose tissue and muscle protein can also result in cytokine induced malnutrition (Beisel 1995), further enhancing the synergistic

relationship between inadequate nutrition and infectious disease. Particularly when these immune responses are prolonged, the individual may suffer increasing levels of physiological stress as well as become more susceptible to other infections. Thus, poor nutrition increases the likelihood of infectious disease and vice versa.

Another pattern sometimes observed is differential rates of enamel hypoplasia and disease occurrence in female children compare to male. Girls were noted to experience generally higher rates of infection as well as more hypoplastic defects compared to boys in the Guatemalan supplementation study (May et al. 1993). However, the high morbidity male group reported fewer defects than the low male morbidity group. The authors explained that not only did unwell boys receive greater supplementation than girls who were ill, but they also received more than males who were well (May et al. 1993:45). Preferential care directed towards male children explains this apparently contradictory pattern, but also emphasises how cultural factors can influence the prevalence and patterning of stress defects. Conversely, in children exposed to the Chinese famine when preferential care of males was known to occur, a higher frequency of hypoplastic defects was found in Chinese males compare to females who had experienced famine (Zhou and Corruccini 1998). These data, however, reflect that preferential male care resulted in relatively more males surviving the famine. If cultural behaviours are not considered, they may have the potential to confound interpretations and lead to inaccurate conclusions about who was most impacted by stressful events.

While studies of living populations have clearly demonstrated a link between physiological stressors involving synergisms between under nutrition, infection, and immune response, bioarchaeological analyses are able to examine potential relationships between stressors experienced at a young age and earlier than expected

ages at death. A number of studies have reported a trend where higher average numbers of hypoplastic defects are evident in individuals who died prior to adulthood compared to those who attained adulthood (Boldsen 2007; Mendez Colli et al. 2009;; Duray 1996; Goodman & Armelagos 1988; King et al. 2005; Miszkiewicz 2015; Slaus 2000; Stodder 1997; Temple 2014; White 1978). White's (1978) study demonstrated that this association between subadult stress and longevity was also evident in earlier hominins, specifically South African australopithecines. Further studies have reported a dose response, where increasing numbers of defects per individual could be associated with progressively earlier ages at death (Goodman and Armelagos 1988; Steckel 2005).

In a study of individuals from Dickson Mound (Illinois, USA), Goodman and Armelagos (1988) noted individuals with more stress free periods (defined as a 6 month period of crown formation free of hypoplasia) lived longer than individuals who had fewer stress free periods. Specifically, they found that individuals with no hypoplastic defects lived to be, on average, 35.8 years old, while those with one stress period averaged 31.6 years and those with two or more stress periods 25.6 years (Goodman and Armelagos 1988:942). Although this age related trend was evident in groups thought to be relatively more reliant on maize and becoming increasingly sedentary (Mississippian Acculturated Late Woodland and Middle Mississippian cultures), the association was absent in an earlier group (Late Woodland period) considered to be semi sedentary hunter gatherers (Goodman and Armelagos 1988; Buikstra and Milner 1991). This suggests that in some situations occurrences of enamel hypoplasia are not always linked to decreased longevity– the relationship appears to vary in different environmental contexts. There are also situations when this general pattern appears reversed, such as in a study of Iron Age individuals in Pella, Jordan. Here, Griffin and Donlon (2009), who were looking at the patterning of different types of hypoplasia,

reported that all adults had hypoplasia compared to 46% of the subadults. This high prevalence in the adult group suggests that none escaped physiological stressors during childhood. In this context, it is likely that the lower frequency of defects in the subadults is consistent with the osteological paradox, a reminder that many who experience stressors are not always able to survive.

Timing of early stressors

A key aspect of life course models, including both critical periods and accumulation models explaining how early and later stressors might be connected, is the role of stressor timing. Accurate estimates of age when physiological stress occurred permit judgements about relationships with subsequent adverse health. The studies reviewed so far have focused on establishing a relationship between the presence of hypoplastic defects and physiological stress as well as describing the synergistic relationship between disease and inadequate nutrition that is so often the cause of this stress. As one of the particularly useful characteristics of enamel hypoplasia is our ability to estimate the age of individuals when they experienced the systemic insults, studies that have included timing in their analyses are now discussed.

While the permanent dentition can record postnatal stress episodes, the deciduous teeth capture information regarding foetal stressors associated with maternal health during gestation. A study analysing deciduous and permanent teeth found that individuals who had experienced prenatal stressors had decreased survivorship compared to those who experienced initial stress during later postnatal periods (Blakey and Armelagos 1985). What is particularly interesting is that age at death of children with evidence of prenatal stress was between one to three years of age, which also

coincides with the timing of defect formation in many of those who lived longer (Blakey and Armelagos 1985: 376). This pattern had also been noted in a previous study by Cook and Buikstra (1979), who analysed deciduous teeth in subadults from the Middle and Late Woodland periods of the Lower Illinois Valley (USA). They found individuals with evidence of foetal stressors had higher mortality rates between one and three years of age, as well as an increased likelihood of lesions associated with anaemia and infection (Cook and Buikstra 1979:657). The co-occurrence of peaks in mortality and age of defects in survivors not only suggests that this age (one to three years) was a dangerous period, but also underlines the association between stress and hypoplasia. Studies such as these are rare, probably because both deciduous and permanent dentitions are required as well as infant and child skeletal material, which due to preservation issues are often underrepresented in the skeletal record. An early childhood peak in hypoplastic defects around three years of age has often been reported in studies, which is sometimes attributed to stressors associated with weaning (i.e. Corruccini et al. 1985; Lanphear 1990; Moggi-Cecchi et al. 1994). Historical and isotopic studies, however, suggest this age peak is usually too late to directly reflect the weaning process (Blakey et al. 1994; Katzenberg et al.1996; Saunders and Keenleyside 1999; Wood 1996).

In many studies that analyse archaeological populations, especially those groups which relied on traditional or unprocessed foods, dental wear can be a major hindrance to assessing early stress defects in adult skeletons. The earliest forming defects will be in the most cuspal or incisal enamel as this is earliest formed, but which is also the first to be lost to dental wear. This is why, for example, Goodman and Armelagos (1988) were not able to record defects occurring before the age of 3.5 years. So although relationships between stress episodes and longevity can, in principle, be established if

adequate evidence is available, earlier stress episodes may not always be detectable. This is of particular concern because many studies of modern populations, discussed previously, suggest that stressors during the first few years of life may be particularly important. Frequently in bioarchaeology, researchers limit their samples to crowns with only minimal wear, but which can impose an age bias as older individuals are most likely to be excluded. However, there has been work on populations with lower rates of dental wear, due to a softer diet, which allows early forming defects, such as those prior to three years of age, to be assessed on adult teeth.

A study by King et al. (2005) examined the patterning of enamel hypoplasia in two post mediaeval London populations to investigate how the two groups might vary and what that variation might imply. Using subadults and young adults (< 40 years), as their crowns were relatively unworn, they were able to capture defects starting from 1.2 years of age (King et al. 2005:550). The authors considered how a number of factors including defect frequency, duration, interval, age at first and last defect, and percentage of crown affected by hypoplasia, might relate to either subadult or adult deaths. However, the only factor significantly associated with earlier mortality was age at first defect (King et al. 2005:553). Other studies have also noted a trend where individuals with earlier occurring defects also have a greater number of defects over all (i.e. Littleton 2005; Temple 2010). For example, Littleton (2005) found that in modern Aboriginal people living in Central Australia (Yuendumu) those who had experienced earlier stressors also had a significantly higher mean number of subsequent defects compared to those who were older at the time of initial stress. These studies suggest that the earlier in life stress is experienced, the greater impact. Furthermore, there seems to be a marked shift after three or so years of age, where this relationship becomes more

variable. Again, this points to the role of stressor timing in the relationship between early health insults and later health outcomes.

Modifying effects of nutrition and socioeconomic status

Analyses of human remains from the Classic Mayan period provide another example of the importance of examining the distributions of defects within narrow age groups. A greater number of hypoplastic defects had initially been reported for subadults relative to the adult sample (Mendez Colli et al. 2009). However, a later analysis of the sample divided the subadults into three age ranges and found the age related association was not maintained (Cucina 2011:110). The author noted that collectively the subadults had more defects on average, but this was heavily influenced by a few individuals with exceptionally high numbers of defects. When the outliers were removed, there was also no significant difference between the adults and subadults (Cucina 2011). The author points out that as his age groups started from four years of age, all the individuals analysed had survived earlier stress periods in infancy and early childhood. This suggests that once individuals have survived these earlier insults, later occurring stressors may not have the same impact on longevity (Cucina 2011). Furthermore, Cucina (2011:113) mentions that this population had good access to food resources. This parallels Goodman and Armelagos (1988) study where the relationship between stress defects and longevity is not so apparent in populations who appear to have access to better nutritional resources. Although under nutrition and disease are frequently co-occurring conditions, it is unclear whether these associations primarily reflect nutritional status or are more related to population density and exposure to infectious disease.

Access to good, or at least adequate, nutrition may be driving a similar pattern seen in an analysis of hypoplastic defects in adults from a historic Canadian cemetery (Saunders and Keenleyside 1999). The authors detected no significant difference in age at death between those with and without hypoplastic defects suggesting no association between childhood stressors and adult longevity (Saunders and Keenleyside 1999). Historical records suggest that this group where predominantly middle to upper socioeconomic class and inadequate nutrition was not considered an issue (Saunders and Keenleyside 1999:518). A commonality between these studies is all groups are claimed to have had access to at least sufficient, if not ample, nutritional resources, suggesting that the long term impact of early stressors may be modified by such access. Specifically, in groups with better access to resources, the impact of early stressors appears to be restricted to subadults, while in poorer groups the impact carries through into adulthood.

A study that demonstrates how social status and environments may influence the long term effects of early stressors includes adult groups from three different social classes (Palubeckaite et al. 2002). The authors recorded hypoplastic defects along with age at death in three Danish and Lithuanian medieval groups that would have experienced different social and environmental conditions: rural, urban and aristocratic (Palubeckaite et al. 2002). They found the aristocratic group had significantly more defects than the rural, but fewer than the urban group, which had the greatest frequency of defects. However, within the aristocratic group, the number of stress episodes an individual experienced in childhood had no impact on longevity although this was a significant factor associated with a younger age at death in both the urban and rural groups (Palubeckaite et al. 2002). Despite the rural group having fewer defects, these were still associated with dying younger in adulthood. The long term impacts of

childhood stressors appear to have been modified by social status. Similarly, socioeconomic status was found to be highly relevant to long term impacts of early stressors in a modern adult Portuguese sample. While hypoplastic defects were found to be negatively associated with age at death, detailed historical records allowed the authors to further examine this relationship further (Amoroso et al. 2014). They found factors, including as socioeconomic status, cause of death (infectious and non-infectious), and year of birth, best explained the relationship (Amoroso et al. 2014). They suggest factors operating over the life course were primarily responsible for a younger age at death – rather than a direct effect of early life health insults (Amoroso et al. 2014).

It is evident from these studies is that the relationship between stressors, hypoplastic defects, and longer term impacts is not straightforward. These studies suggest that not only is the number of stress episodes a factor influencing age at death, but the age when stressors are experienced is also an important factor. Cultural contexts and socioeconomic status appear to be able to shift or modify relationships between childhood stress episodes and longevity, including how strong its influence is and how long it may last across the life course. Although physiological stressors have a biological basis, who is exposed and to what degree is often socially mediated. Furthermore, it is also possible that adequate nutrition, or better access to resources in general, across the life course may play a particularly important role in governing longer term impacts. These studies emphasise that in order to fully understand relationships between early and later life health outcomes, considering the timing and frequency of early stressors along with insight into the wider environmental and socioeconomic context are imperative.

3.2.3. Femoral and tibial lengths

Another lens through which the early environment may be glimpsed in skeletal remains is in the final length achieved by long bone growth, particularly the femur and tibia. Variation in the length of these bones is responsible for most of the variation in stature (Bogin and Varela-Silva 2010). A number of studies using living people have linked variation in adult stature to environmental conditions experienced during subadult development and is considered a useful proxy for gauging the health status of a group or population (Steckel 1995; Haines 2004). Understanding the nature and timing of growth of these distal long bones may allow an understanding of the ages when physiological stressors are most likely to impede their growth. This, in turn, allows me to use timing and frequency of stressors as indicated by hypoplastic defects to estimate the likelihood that permanent stunting accrued in the long bones of adults.

Whether an individual is able to achieve their potential in long bone length depends on exposures to growth faltering episodes during development, of which nutrition and disease are likely to be key (Martorell et al. 1975; Ulijaszek and Strickland 1993). For example, work by Floyd and Littleton (2006) examining the longitudinal relationship between the timing of hypoplastic defects and subsequent growth in an historic Aboriginal population pointed to the importance of stress occurring at particular periods of childhood development. Essentially growth is a plastic process, which means that growth rates can vary in response to developmental conditions, allowing energy to be prioritised towards functions more essential for survival, such as brain growth (Bogin 1999). From about six months of age to around seven years in females and nine or 10 years in males, the lower legs grow faster than any other body segment (Bogin and Varela-Silva 2010). This fast pace of growth means that leg length is particularly responsive, or vulnerable, to adverse conditions, with the

tibia suggested to be particularly sensitive to environmental conditions (Jantz and Owsley 1984; Holliday and Ruff 2001; Smith and Buschang 2004; Bogin and Varela-Silva 2010).

In skeletal material, variation in growth processes has been investigated cross sectionally using long bone lengths of subadult individuals across a range of ages. A study comparing variation in tibial growth between two subadult groups (Late Woodland and Late Archaic sites) found that the group likely exposed to higher levels of disease exposure showed delayed tibial growth (length) between six months to four years of age, with the greatest difference occurring between one and two years of age (Mensforth 1985). However, when age related changes in subadult femora and tibiae were investigated from early and late Neolithic sites in the Cis-Baikal region, the femur was found to be more indicative of stressors (Temple et al. 2014). This was suggested to relate to the timing of stressors in relation to the differential timing of growth velocities between the femur and tibia (Temple et al. 2014). Analysis of longitudinal data from the Denver Child Research Council found that tibial peak velocity occurs slightly prior to peak velocity in the femur, on average, but the greatest difference in timing occurred between the sexes, with females reaching peak velocity for both tibia and femur approximately two years, on average, earlier than boys (Smith and Buschang 2005). In general, proximal limb segments grow at a greater velocity relative to distal segments, which for leg bones means that the femur grows more rapidly than the tibia (Smith and Buschang 2004; 2005). However, despite this greater rate of growth in the femur, the tibia was found to be consistently more variable in growth, particularly in females (Smith and Buschang 2004; 2005). The authors point out that this is consistent with female growth being more canalised as well as demonstrating that the tibia is more sensitive to environmental impacts (Smith and Buschang 2004; 2005).

In adult skeletal remains, variation in stature, or femoral and tibial lengths as proxies, can provide useful information about developmental conditions. This can allow groups that experienced suboptimal conditions during growth can be identified (Steegmann 1985; Eveleth and Tanner 1990; Steckel 1995; Floyd and Littleton 2006). In bioarchaeology, stature has allowed variation in developmental conditions to be linked to socioeconomic disparities (Kemkes-Grottenthaler 2005; Maat 2005; Vercellotti et al. 2011) and shifts in cultural practices influencing developmental environments, such as the transition to agriculture and industrialisation (Cook 1984; Goodman et al. 1984; Pietrusewsky and Douglas 2001; Lewis 2002; Pinhasi et al. 2006, 2011; but see Mays, Brickley, and Ives 2008 for conflicting findings regarding industrialisation), with the most common denominator being nutrition and disease exposure (Larsen 1997; Bogin 1999).

A study also using post medieval London material, compared adult tibial and femoral lengths from Chelsea and Farringdon (high and low socioeconomic status sites) to gauge how these measurements related to age at death in differing social groups as well as by sex. Variation in long bone length was not related to age at death for any group, but the high status females were found to have significantly longer femora compared to lower status females. No significant differences were detected between high and low status males (Hughes-Morey 2016). However, the author considered long bone lengths below one standard deviation from the sex specific mean to be stunted (Hughes-Morey 2016:3), which invokes an aspect of the ecological fallacy. This occurs when population or group level data is used to directly, but erroneously infer something about the individual (Schwartz 1994; Diez-Roux 1998). In this situation, circular logic also underlies the assumption that only those below one standard deviation are stunted as it also assumes that only the genetically short can become stunted. This ignores the

likelihood that genetically taller individuals are just as likely to have experienced growth faltering episodes, but may still have a final stature that is average or above. This is a particularly reasonable suggestion considering that, even when statistically significant, a shift in mean stature values is frequently small (~ 2 cm) (Garn et al. 1975). Therefore, it is possible that the majority of individuals who experienced growth faltering are not recognised as 'short'. This represents a serious potential confounding of results from this type of analysis. Variation between group means in stature can detect real differences and reliably infer something about variation in developmental conditions between groups if we can reasonably assume common ancestry, but it cannot detect which individuals are responsible for the shift.

Using hypoplastic defects, Temple (2008) detected differences in stress levels using between eastern and western Jomon groups, but stature did not differ significantly. He suggests either stressors were not sufficient to cause growth faltering or may have been alleviated by catch-up growth. Conversely, within western Jomon differences in stature were evident between the Middle and Late to Final periods, but the frequency of stress indicators did not change (Temple 2008). The author acknowledges that the relationship between hypoplastic defects and stature may not be straight-forward (Temple 2008). In bioarchaeology, evidence of growth faltering can be elusive, but also the absence of skeletal or dental stressors does not necessarily imply ideal developmental conditions were experienced (King and Ulijaszek 1999). Ribot and Roberts (1996) compared long bone diaphyseal lengths of children who exhibited low numbers of nonspecific stress indicators (cribra orbitalia, Harris lines, enamel hypoplasia, and periosteal new bone formation) with those who had more and found no apparent relationship. The authors point out that the frequency and duration of stress episodes may not always be sufficient to cause growth faltering, but also assessments

may be complicated by catch-up growth (Ribot and Roberts 1996). The authors suggest that additional assessments such as cortical thickness might provide a fuller picture of trade-offs between long bone growth and physiological stressors. The importance of cortical thickness is also expressed by Mays (1999) who suggests cortical thickness may be a more sensitive assessment of growth faltering. Cortical thickness is the result of two processes: bone formation and resorption. Appositional growth of sub periosteal bone causes overall bone thickness to increase, while resorption of the endosteal surface widens the medullary cavity, but periods of endosteal bone formation will also occur as well (Mays 1999). This means, unfortunately, that cortical thickness cannot be reliably assessed from external bone dimensions as the size of the medullary cavity also needs to be considered. This requires radiographs or destructive sectioning. These studies suggest the relationship between stature or long bone length and stressors is not straight forward, but is likely influenced by other unseen factors.

Possible confounders that can influence the relationship between stressors and final height or length attainment is catch-up and compensatory growth. Improved conditions can allow individuals to undergo catch-up growth, when the growth rate is accelerated following a short term interruption, such as under nutrition or illness, allowing the individual to reach the same size they would have been without the health insult (Bogin 1999). Although sometimes mislabelled as catch-up growth, delays in skeletal maturation that accompany reductions in the pace of growth may experience delayed or extended growth periods, as during adolescence, allowing a greater final height to be achieved (Golden 1994). However, catch-up growth (as a measureable phenomenon) is suggested to be more associated with short term growth interruptions while final adult height reflects more chronic conditions (Bogin 1999). In addition, adequate levels of nutrition are required for catch-up growth to occur (Golden 1994;

Prentice et al. 2013). Individuals who remain in the environment in which growth faltering occurred tend to experience little to no catch-up growth (Martorell et al. 1994).

Final femoral and tibial length attained is likely a net account of growth deficits and catch-up periods, potentially making interpretations of the childhood environments difficult. Despite these issues, however, they may still provide useful insight into how development conditions may have varied between socioeconomic groups, particularly between the most extreme groups.

3.3 Adult stress indicators

3.3.1 Periosteal new bone

Periosteal new bone formation refers to new bone produced by the periosteum, the fibrous membrane covering the outer surface of cortical bone. The periosteum is composed of two layers: an outer fibrous layer and an inner osteogenic layer that contains progenitor cells as well as mature osteoblasts (Dwek 2010). It is highly vascular, supplying blood to the bone and is particularly sensitive to disruption to which it responds by forming new bone (Dwek 2010). Such disruptions, or insults, might include inflammation in surrounding tissue, haemorrhages, trauma to the membrane itself, or any situation where the membrane is lifted from the bone surface, such as with osteogenic tumours (Roberts and Manchester 2007; Schultz 2001; Ortner 2003; Weston 2008; Waldron 2009; Mays 2010). In skeletal remains, the precise cause of periosteal new bone is usually unknowable as it can be part of complex disease processes, although frequently lesions are considered due to a combination of trauma and infection (Schultz 2001; Ortner 2003).

Periosteal new bone is most commonly reported on the tibia (Larsen 1997). This may be due to the tibial receiving more trauma, such as knocks to the lower leg, as the anterior surface of the bone is relatively unprotected by muscle or fat tissue, or to a lower surface temperature making it more susceptible to infection (Roberts and Manchester 2007). In addition, bones can vary in their ability to produce periosteum new bone, for example, the tibial periosteum has greater osteogenic potential than that of the calvarium (Dwek 2010). In studies that selectively score the tibia for periosteal new bone, a high percentage of lesions may result from trauma rather than systemic origin such as disease processes – possibly confounding interpretations of adverse health levels in the populations (Weston 2008). However, the patterning of lesions may help differentiate between trauma and disease, as single occurrences are more likely be due to trauma (Ortner 2003). Multiple lesions may mean an infection has spread from an initial infection, while bilateral lesions may be more likely to be associated with systemic diseases (Ortner 2003; Weston 2012). However, these are only suggestive and it is important to remember that infection may result from trauma, and trauma itself may be related to behaviour (Larsen 1997). Another confounding factor concerns age, as the healing process is prolonged in older adults (Boskey and Coleman 2010), higher frequencies scored in these age groups may reflect normal age related changes in remodelling rates.

The appearance of periosteal new bone lesions vary by stage as they progress from active formation to remodelled cortical bone. When first formed, the new bone is produced quickly and has a haphazard appearance, known as woven bone (Ortner 2003). The new bone has the porous appearance of pumice and may lie as plaque on the cortical surface or as fine striations (Ortner 2003; Weston 2008). Sharp edges denote that no remodelling has occurred meaning new bone formation was active at the time of

death. Remodelled periosteal new bone will have rounded edges and may be developing areas of smooth dense lamellar bone within the lesion, which increase in area as the healing process continues (Weston 2008;). Healed lesions demonstrate that the individual survived the period of initial inflammation and lived long enough for bone remodelling to begin. Some lesions may show a mix of the two states; active new bone alongside remodelled regions. This state may suggest that the lesion is associated with more chronic, or ongoing, inflammation, particularly when active new bone was still being produced (Roberts and Manchester 2007).

The relationship between periosteal new bone and adverse health has been well documented in a number of studies suggesting a link with increasing population density that points to the role of infectious agents (Larsen 1997). For example, high frequencies were reported in an urban Medieval York population (Grauer 1993), while lower occurrences where noted in rural Wharram Percy (Mays 2010). Furthermore, while frequencies in the urban group increased with age, they also tended to be remodelled, indicating survival, while at Wharram Percy more were active at the time of death (Grauer 1993; Mays 2010). This could suggest those living in the city may have been exposed to a greater number of infectious agents across their lives and thus more likely to survive subsequent infections (Mays 2010). The association between healed lesions and increased longevity was also noted in a number of London medieval samples, suggesting their usefulness in identifying frailty in different age groups (DeWitte 2014). DeWitte (2014) found a clear signal where marked decreased survival was linked to active lesions, while those with healed lesions were the longest lived – supporting the notion of healed lesions as a sign of survival and possibly decreased frailty. Although periosteal new bone lesions may be caused by a number of conditions, they indicate the presence of inflammation. Furthermore, lesion state at death may also be useful in

identifying groups more likely to have survived causal stressors. Considering these lesions along with other skeletal stress indicators, such as periodontitis, and age at death may help identify differential levels of frailty within a sample.

3.3.2 Periodontitis

Periodontal disease is an inflammatory condition that affects supporting tissues surrounding teeth. Specifically, these structures include the alveolar bone, periodontal ligament, cementum, gingivae and the mucosa (Cochran 2008). Bacterial infection is the underlying cause of periodontal disease, involving a variety of opportunistic species commonly found in the oral environment (Cochran 2008). If bacterial growth becomes excessive, an inflammatory response, via the innate immune system, is initiated (Cochran 2008). Initially, inflammation is restricted to the gingiva, known as gingivitis. At this stage, the underlying alveolar bone is not affected, but if the inflammation is prolonged, or reoccurring, it can result in increased osteoclastic activity and subsequent bone resorption (Armitage 2004; Cochran 2008). Once alveolar bone is involved the condition is termed periodontitis. Two types of periodontitis are recognised: chronic and aggressive. In dentistry, the term 'aggressive periodontitis' is often reserved for a rare rampant form predominately affecting adolescents, as opposed to the more common 'chronic' form usually only found in adults (Armitage 2004). Clinically, chronic periodontitis is classified as mild, moderate, or severe – depending on the amount of bone loss that can be estimated using a dental probe or radiographs (Armitage 2004). Severe periodontitis is recognised by the formation of deep interdental pocket lesions. A particular advantage of periodontal disease is that its form and severity are easily recognisable in dry bone.

Over the last several decades there has been a growing body of research linking chronic periodontitis with systemic disease in living people, suggesting a close link with chronic adverse health. Periodontitis was first noticed to be a common co-morbidity with diabetes mellitus – particularly type 2, and subsequent research has identified a synergistic relationship between the two conditions (Nelson et al. 1990; Scannapieco et al. 2003a; Chavarry et al. 2009; Preshaw et al. 2012). Furthermore, severe chronic periodontitis is considered a risk factor for various systemic diseases including heart disease, stroke, osteoporosis and renal dysfunction (Naugle et al. 1998; von Wowern et al. 1994: Morrison et al. 1999; Garcia et al. 2001). This disease has also been found to be strongly associated with individuals who have impaired immune systems including those who have an immunodeficiency disorder (e.g. HIV) as well as those who are immunosuppressed due to organ transplants (Swango et al. 1991; Seymour et al. 1997; Varga 1998). In addition, periodontitis has also been implicated as an infectious source for pulmonary diseases, including bacterial pneumonia and chronic obstructive pulmonary disease (Hayes et al. 1998; Limeback 1998; Scannapieco et al. 2003). Although periodontal disease is not considered directly causal to these conditions, periodontal pockets are suggested to act as bacterial reservoirs for many of these infections (Garcia et al. 2001). However, other research suggests latent or chronic infections may alter systemic levels of inflammatory mediators, possibly causing a hyper-inflammatory state (Barton et al. 2007).

Recent *in vitro* work not only suggests how periodontitis may be linked with other chronic diseases, but also highlights its relevance to bioarchaeology. This study found exposing peripheral blood mononuclear cells from healthy donors to *Mycobacterium tuberculosis* or *M. leprae* elicited a shift in inflammatory markers when subsequently exposed to *Porphyromonas gingivalis*, a bacterium implicated in

periodontitis (Crespo et al. 2016). This increase in Th1 proinflammatory cytokines, resulting in a heightened inflammatory response, may explain why individuals with chronic disease are also likely to experience more severe periodontitis. As a proxy for inflammatory competence, the authors propose that the severity of periodontitis lesions may prove a useful indicator of health status in archaeological populations (Crespo et al. 2016:153). Overall, these studies suggest severe periodontitis may be linked to impaired immune systems. It is this propensity that points to its potential as a marker of chronic adverse health in skeletal remains, possibly allowing more subtle adverse health conditions to be identified than reflected in age at death.

However, in addition to chronic disease, periodontitis is also associated with sex, social factors, such as poor nutrition, and behaviours including the use of tobacco products (Clarke and Hirsch 1995; Poulton et al. 2002; Pihlstrom et al. 2005), which also need to be considered as possible risk factors when attempting to interpret lesion distributions. A study that considered a number of potential risk indicators for severe periodontal bone loss found the strongest risks were age and smoking, both of which displayed a particularly strong dose response (Grossi et al. 1994; Grossi et al. 1995). In addition, males were also slightly more likely than females to have periodontitis (Grossi et al. 1995; Shiau and Reynolds 2010). Although the reason for this is unclear, it is suggested to reflect sex specific differences in immune function host susceptibility (Grossi et al. 1995; Shiau and Reynolds 2010).

In bioarchaeology, comparative periodontitis studies have been hindered by different scoring techniques. Methods that assess the degree of periodontal destruction by measurements of alveolar crest height are thought to over-estimate the amount of bone lost and therefore the occurrence of periodontitis in archaeological samples (Clarke et al. 1986). This was a particular problem when assessing horizontal bone loss

in worn dentitions due to continuing eruption (Hilllson 1996). Kerr (1988) developed a scoring system that assesses the inflammatory response of the bone itself and destruction of the interdental septa that resolved this issue. An assessment of periodontal disease in medieval Scottish and post medieval London samples supported initial concerns regarding over estimations (Kerr 1988, 1991, 1994). This work, and more recent analysis using Kerr's system to investigate an historic Portuguese sample (Wasterlain et al. 2011), report similar age related patterns and degrees of severity as seen in modern populations. In addition, both Clarke et al. (1986) and Kerr (1994) doubt the common assumption that periodontal disease was a major cause of ante mortem tooth loss in the past. In support, Wasterlains et al.'s (2011) study revealed an inverse relationship where periodontitis decreased as ante mortem tooth loss increased with age.

A potential confounder when investigating connections between periodontitis status and mortality in archaeology samples is its association with age. In addition to older individuals having had more time to accumulate quiescent lesions, the risk of periodontitis increases independently with age (Kerr 1991, 1994; Hillson 1996; Wasterlain et al. 2011). Therefore, studies that report apparent associations between increased risk of periodontitis and age at death may be reflecting a parallel relationship with age, rather than an independent risk of death. Periodontitis was investigated as a potential indicator of frailty in a medieval London sample, and the authors report a slightly increased risk of death associated with periodontitis and caries (DeWitte and Bekvalac 2010). Although they assessed the condition by measuring the alveolar crest, they did find not particularly high rates of the disease. However, it is possible their association reflected parallel risks, with periodontitis more likely in older individuals who were also independently at greater risk of death. To best establish its use as a

frailty indicator, differentiating between chronic and more severe pocket lesions, such as with Kerr's (1988) method, may prove more reliable.

3.4 Conclusion

Collectively, data gathered from skeletal indicators of stress and supplemented with historical and archaeological information should provide insight into the types of environments individuals examined in this research experienced both as children and adults. At the group level, this means that possible variation in disease and mortality risks may be linked to socioeconomic position, suggesting how social differences might influence mortality profiles and age at death. Considering how these risks might differ between early and later environments means the direction of the relationship can be identified. For example, if the risk of adversity (death or disease) is high in the early environment is it then associated with a higher or lower risk in adulthood? The direction of this relationship can point to mechanisms shaping adult mortality profiles, such as scarring or acquired immunity and selective mortality or correlated environments, as outlined in the model by Preston et al. (1998). In turn, these can help untangle linkages between early and later health outcomes and suggest which life course model, as defined by Ben-Shlomo and Kuh (2002), might be applicable. For example, adult health outcomes might be best explained by an accumulation life course model, when indirect and indirect stressors have accrued across the life course, or alternatively, outcomes might be primarily driven by early stressors occurring during critical periods.

Because analysis of enamel hypoplasia will allow the age when individuals experienced stressors as children to be estimated, this research should be able to detect the role of stressor timing in later health outcomes. This means the ages during

childhood when individuals might be more vulnerable to long term impacts of stressors can be determined. Considering if age related outcomes are influenced by socioeconomic group or sex may suggest whether such vulnerable ages represent critical or sensitive periods, where later impacts are able to be modified. Alternatively, this analysis may determine that the frequency of childhood health insults is more relevant to adult health than the specific ages when they were experienced. Identifying and defining how childhood health insults might relate to adult health risks will help expand our understanding of how and in what circumstances early stressors can impact later life.

CHAPTER FOUR: MATERIALS AND METHODS

4.1 Introduction

This chapter is divided into two main sections, materials and methods. First, context and information is provided for the skeletal samples used in this research. It begins with an overview of London during the Industrial revolution, as this very much sets the scene for the lives of individuals used in this investigation. The individual cemetery samples are then described, including socioeconomic status and other useful information from previous skeletal analyses that might help contextualise the differing environments in which these individuals lived.

The second section of this chapter deals with methods used to record dental and skeletal data, but also details data gathered form parish burial records used to supplement skeletal information. Methods for recording dental and skeletal stress indicators pertaining to childhood health experiences are explained first, followed by skeletal lesions associated with adulthood morbidity. Following this, techniques and approaches used to establish age at death and sex for the skeletal samples are explained, along with their distribution. The collection of data from parish burial records is then described, which includes information on mortality for all age groups. Lastly, an overview of statistical approaches and tests used, including survival and risk analysis, are then briefly outlined.

4.2 Materials and context

4.2.1 London and the Industrial Revolution: Social and health aspects

Considering the temporal context in which people lived is vital to understanding the type of health risks they may have experienced, including how homogeneous these hazards might have been. The skeletal material used in this research are the remains of individuals who lived in London between 1673 and 1852. This means they lived and died during an age of immense social change driven by the Industrial Revolution - a period characterised by increasing urbanisation, migration, and growing disparities in wealth.

For at least the last thousand years, London has been a magnet to migrants – from rural Britain and abroad. Positioned on the upper tidal reaches of the River Thames, London and its port has been the main focus of inland trade since the 12th Century (Schofield and Vince 2003). Since the Late Middles Ages (1301–1500) trade underpinned and propelled London's growth in both population and wealth, creating a constant demand for labourers (Landers 1987). Most migrant workers originated from rural regions and were often immunologically naïve to diseases endemic in London **(**Landers and Mouzas 1988). For example, analyses of the Bills of Mortality (a weekly record of all London deaths, originally actioned to monitor plague outbreaks) report a positive correlation between rising grain prices and increased deaths from smallpox and 'fevers', particularly affecting young adults. The inference from this being that crop failures pushed migrants to the city to escape rural hardships, increasing their risk of exposure to infectious disease (Galloway 1985; Landers 1987).

The first phase of the Industrial Revolution (1760 -1880), fuelled by the invention of the steam engine, resulted in the industrialisation of labour and factory

based manufacturing (Stearns 2012). Previously, manufacturing had been at a cottage level (for example, weaving) and the technological shift created a huge demand for factory workers. This demand drew rural people to the growing towns and cities – including London (Stearns 2012). Along with an economic boom for England, the Industrial Revolution heralded many social changes: including the growth of a wealthy entrepreneurial middle class and the creation of a much larger lower working class 'factory worker' (Stearns 2012). As the increased average wage rose, the population density in cities also grew - placing heavy demand on infrastructures not designed to cope with such numbers; namely housing, water, and sewage.

The Industrial Revolution saw a rise in demand for both male labourers and female domestic workers, resulting in a high proportion of London's population being young adults (Williamson 1988). The 1821 census for London, for example, showed a peak for individuals in their 20s that was nearly 10% higher than the rest of England (Davenport et al. 2010). In addition, large tracts of land that had been previously farmed by tenant farmers were now turned to cash crops by owners – displacing rural families of both home and income and forcing many to migrate to London or elsewhere (Williamson 1988). London's population had grown steadily from the 1500s with growth largely attributed to immigrants (Landers 1991). Based on baptism and burial records, a net surplus of baptisms only occurred in London after the 1790s, but which then grew exponentially (Landers 1991). London's infrastructure was unable to adequately cope with the increasing demands, forcing many to live in overcrowded and unsanitary conditions (Williamson 1988).

Although, in general, life expectancy improved in London over the 1800s, this was not uniform across the population (Landers and Mouzas 1988; Razzell and Spence 2005). Mortality rates, particularly for infants and children, followed population

density; areas with greatest density, which were also the poorest. These overcrowded areas had the highest mortality rates - driven by increased risk of exposure to pathogens (particularly person to person) as well as inadequate sanitation and waste disposal (Huck 1995; Landers 1991). The city provided ideal conditions for many infectious diseases; around 10% of infants and children are estimated to have died from smallpox (*Variola major*) alone in the latter half of the 1700s, while deaths from tuberculosis (*Mycobacterium tuberculosis*) were almost double that during the same period, but which grew even worse as the turn of the century approached (Landers and Mouzas 1988). Tuberculosis spread rapidly across the seventeenth and eighteenth centuries, peaking in the year 1800 (Murray 2004). For London, as in many other cities, the social conditions created by the Industrial Revolution ensured its continued rampage (Frith 2014). The impact of tuberculosis on the population was massive; at the end of the 1700s – a quarter of all deaths recorded in parish registries for England were attributed to tuberculosis, which is likely an under estimation (Frith 2014). These figures, however, played out differently across social strata; the poor were disproportionately impacted as not only were their living conditions and risk of exposure greater, but health care afforded by the wealthy was beyond their reach (Frith 2014).

The Industrial Revolution created a socially bipolarised London; for the successful middle classes, access to good housing, nutrition, and health care made their lives somewhat more comfortable than conditions experienced by the poorer working classes. While social groups are often simplified to two extremes (for example, rich and poor), it was actually a continuum where outcomes were influenced by where members of a group were situated. Furthermore, the spatial divisions are not always particularly evident, even within a single parish. While some wealthy families lived away from the unsanitary and overcrowded city – in more pleasant semirural surroundings, such as

Chelsea; others often lived nearer or at their places of business in the city, such as in the commercial area around Fleet Street. Within the city, wealthy and poor frequently lived next door to each other – as respectable, or even grand, houses could be found in streets that led to overcrowded allies and tenements. The skeletal samples used in this research are of individuals who belonged to differing socioeconomic groups, providing a gradient from the poorest workhouse residences to wealthy business owners. In addition, the samples include groups who resided in the heart of the commercial area, but also in the suburban areas, outside the densely populated city. During this period, it is likely that most people experienced high levels of disease exposure, particularly tuberculosis. In this case, the status advantage might lie in the ability to resist or slow progression, if not overcome the disease, due to greater immunological function afforded by better nutrition and health care. Therefore, considering how socioeconomic status might influence variation in health outcomes is particularly germane. A further consideration is how migration might impact apparent associations between early and later life health outcomes. The skeletal samples will likely vary in their composition of individuals who were raised in London or migrated as adults from rural regions– something that is unknowable from the available data, but will need to be considered when interpreting results.

4.2.2 The skeletal samples

The skeletal samples originate from four different burial grounds in three parishes shown in Figure 4.1. All are curated by The Centre for Human Bioarchaeology, which is part of the London Archaeological Archive and Research Centre (LAARC). Chelsea Old Church, St. Benet's Sherehog, and St. Bride's Lower

collections are housed at the Museum of London, while the St. Bride's Crypt collection is housed in the crypt under St. Bride's Church, Fleet Street. The samples range across broad socioeconomic divides and their experiences of life, and London, were probably very different. I am interested in how their childhood health experiences may have impacted or shaped their adult life expectancy, and how their social status may have mediated these outcomes.

Figure 4.1 Map of London and environs in 1831 showing locations of cemetery sites. 1= Chelsea Old Church, 2 =St. Brides crypt, 3 St. Bride's Lower (Farringdon), 4 = St. Benet's Sherehog. Image courtesy of University of Essex 2004.

Prior to my field trips, individuals from St. Brides Lower (Farringdon), Chelsea Old Church, and St. Benet's Sherehog, were selected from the Wellcome Osteological Research Database (WORD 2016), which holds skeletal data for many of the collections curated by the Museum of London. My intention was not to construct demographic profiles of the once living populations, but to address specific questions relating childhood to adulthood health outcomes at an individual level, so it was

important that all adult age groups were represented, especially the older individuals. It was also essential that individuals had reached adulthood, retained at least one mandibular canine, and were in a good state of preservation with at least the crania, innominate, and femur or tibia present. A stratified sampling approach was used to select at least 100 individuals meeting the above criteria for each of the three sites, which involved selecting individuals evenly spread across each site's list.

At the time of recording, many of those originally selected where found to have essential data unrecordable, for example a mandibular canine may have been present, but too damaged to be reliably assessed, therefore Table 4.1 reports only final sample sizes. The lists generated by WORD (2016) were in numeric order based on catalogue numbers, but were already random with respect to criteria used. Note that two separate collections originate from the one parish of St. Bride's; St. Bride's crypt collection are individuals originally interred within the church, while St. Bride's lower collection were interred in the lower burial ground in Farringdon Street and is referred to as the Farringdon sample. The Bride's crypt collection was offered to me, unexpectedly, during the second visit so these individuals had not been previously selected. This collection is housed in the church's crypt and selection, by necessity, was based on accessibility of individual storage boxes (these were not ordered by any particular criteria). All accessible individuals were recorded if my selection criteria were met. The number of individuals recorded from each site, along with internment dates are presented in Table 4.1.

Table 4.1 Cemetery samples including site, location, and date range for burials and number of individuals.

Cemetery Site	Site Location	Burial Dates	Social Status	No. Individuals
St. Bride's Crypt	St. Bride's, Fleet St. EC4	1740-1852	High	41
Chelsea Old Church	2-4 Old Church St. Chelsea	1700-1850	Medium/high	59
St. Benet's Sherehog	1 Poultry, EC2	1673-1827	Medium	45
St. Bride's Lower (Farringdon)	75-82 Farringdon St. EC4	1770-1849	Low	50

St. Bride's crypt

St. Bride's church is located just off Fleet Street and archaeology suggests there has been a church on the site continually since at least the 7th century, involving seven replacement churches. Prior to post WWII rebuilding work in the 1950s, 227 coffin burials were excavated from within the church, including coffin plates (example Figure 4.2). These were dated from the mid-1700s to mid-1800s (Scheuer and Bowman 1995).

Figure 4.2 Lead coffin plate of Judith McFarlane, died 17th July 1832 aged 60 years

Fleet Street was the focus of a busy commercial and retail area, known for its association with the printing and publishing industry. The individuals who comprise the crypt collection represent the wealthier families of the parish. Not only was it more expensive to be buried within the church, but parish records show an array of noteworthy people, including a Lord Mayor of London, members of parliament, titled individuals, professional and businessmen of note and their families. Although this skeletal sample represents individuals of relatively higher socioeconomic status compared to the other samples used in this research, they lived in a crowded commercial area where poor and wealthy lived side by side. For example, a survey of the St. Bride's burial register reveals in one small area off Fleet Street, Peterborough Court, high status individuals, who could afforded to be buried in the aisle and vaults within the church, were just as likely to reside in the court as those from the workhouse,

which was also located in the court. A further example of this juxtaposition is provided by a public health proponent writing at the time: "Immediately behind rows of the best constructed houses in the fashionable districts of London are some of the worst dwellings, into which the working classes are crowded; and these dwellings, by the noxious influences described, are the foci of disease" (Chadwick 1842:92).

Most of the crypt skeletal collection is comprised of adults, with the greatest number of individuals dying in their sixties, while just over 10% were under twenty years. This proportion of subadults is lower than the number recorded as buried within the church (26%), while in the wider parish, including St. Brides Lower (Farringdon), 40% were under 20 years (Scheuer and Bowman 1995). This difference may have arisen due to recovery bias during excavation, or alternatively, reflect the composition of the higher status population in St. Bride's parish. For example, wealthier families may not have considered the commercial area particularly desirable for raising children. Although St. Bride's coffin plate collection has been the focus of a number of investigations regarding age and sexing, little has been reported on the health of this groups, other than dental pathology. In summary, this is a collection of predominantly high status individuals, but who lived in the heart of a densely populated urban area, often alongside poverty and squalor.

Chelsea Old Church

Excavations were carried out in 2000 at the site of All Saints Chelsea Old Church following the demolition of the old vicarage in advance of rebuilding (Cowie et al. 2008). Based on their location within the burial ground as well as dates from a number of lead coffin plates and burial furniture styles, most burials date from 1700 to

1850 (Cowie et al. 2008). Of the 290 burials recovered, 198 individuals were recordable and data entered into the WORD database. Prior to the 1700s, Chelsea had been a rural riverside village with easy access to Westminster and the city via the river (Figure 4.3). By the early 1700s, however, the village had grown substantially into a London suburb with approximately 300 houses, although still with a rural aspect surrounded by fields and orchards. (Cowie et al. 2008). By the 1800s it had become increasing urbanised as new streets continued to replace agricultural land.

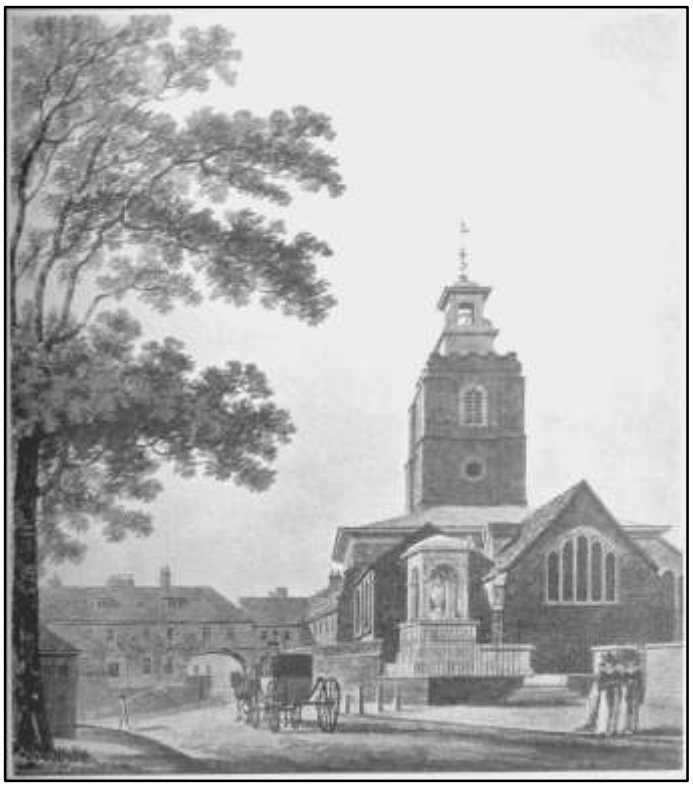

Figure 4.3 Chelsea Old Church in the 1800s by Walter H Godfrey (British History, Online Version 5).

Chelsea was outside the City of London so not included in the Bills of Mortality or the London census, making it more difficult to assess actual social and mortality distributions of the village. However, skeletal analysis undertaken by the Museum of London suggests that the percentage of subadults appears relatively low compared to other London parishes at the time, with a greater proportion probably surviving into

older adulthood (Cowie et al. 2008). This could possibly reflect a generally lower risk of disease exposure due to its more rural location. But despite being situated outside London, its residents were still susceptible to tuberculosis. Analyses by the Museum of London showed vertebral lesions highly consistent with tuberculosis infection in several individuals (Cowie et al. 2008). These occurrences were lower than those observed in other London skeletal collections from the same period, tentatively suggesting that tuberculosis might have been experienced less frequently than in urban London (Cowie et al. 2008). In addition, most of its residents were probably reasonably wealthy, with archaeological evidence describing a middle to upper middle class population able to afford to live in a growing suburb that allowed easy access to the City while avoiding many of its problems. Conversely, the presence of a workhouse (built in 1737) suggests that the population was likely more a mix of wealthy and poor, and would have included lower paid agricultural and factory workers (Croot 2004; Cowie et al. 2008).

St. Benet's Sherehog

Archaeological excavations at 1 Poultry were carried out in 1994 preceding redevelopment work at this site, which uncovered the burial ground and remains of St. Benet's Sherehog Church (Miles and White 2008). The church itself was destroyed in the Great Fire of London of 1666, but the burial ground continued to be used until 1853 as the parish was amalgamated with St. Stephen's Walbrook in 1670 (Miles and White 2008). Burial records suggest that most individuals were interned in the first half of the 1700s; after 1750 numbers decreased until the last burial in 1827 (Miles and White 2008). St. Benet's Sherehog was situated within London's square mile, with the commercial nature of this area evident in Figure 4.4.

Figure 4.4 View from Poultry looking along Cheapside in 1823 showing the commercial nature of this district, St. Benet's site is immediately behind the building in the left foreground (drawing by W. Duryer, Wikimedia Commons).

The parish was small compared to others in London, covering just 0.43 hectares. The 1695 Poll tax records show that 76 householders and 44 lodgers resided in the parish (Miles and White 2008). The 230 excavated individuals, dated after the Great Fire, may represent most of the actual burials that took place in this period, as little truncation or disturbance from encroaching burials was evident (Miles and White 2008). Based on burial records, St. Benet's appears to have had a lower percentage of child deaths (2 -10 years) compared to London in general, but an unusually high percentage of adolescent deaths (11 – 20 years), possibly reflecting the number of apprentices employed in the area (Miles and White 2008). Previous skeletal analysis

also suggests an excess of males relative to females in the assemblage (ratio = 1.31, Miles and White 2008). The social status of most individuals here may be described as 'middling', neither very poor nor particularly wealthy. Dominant occupations listed in Poll tax data record many as 'merchant' as well as a variety of trades and professions from attorneys and law clerks to bee keepers. (Miles and White 2008).

St. Bride's Lower, Farringdon

Also excavated in advance of building work, a second burial ground associated with St. Bride's Church uncovered 606 burials, of which 544 are curated by the Museum of London (Kausmally 2008). St. Bride's Lower cemetery at 75 Farringdon Road was opened during the 1700s as an overflow to the upper burial ground surrounding St. Bride's church and was some distance from the church itself (Miles 2010). This was not a place people choose to be buried and historical accounts from the time describe the burial ground as frequently in a dreadful state of overcrowding with stacked burials and unmaintained grounds where nefarious activities took place (Miles 2010). However, it was inexpensive to be buried here. It was also where the church buried for the poorest of the parish, such as those from workhouse, who could not afford to pay. Parish burial records show that between the years 1783 and 1798, 1731 burials occurred in the lower ground, of which 64% were gratuitous (ground provided for free). Most of the remaining individuals are from the many densely populated allies and courts in the parish. Poverty here was described as dire; labourers' houses often lacked a water supply, adequate sewerage (some had cesspools in their cellars or shared one toilet between many houses) and often had between fifteen to twenty people in one house – sometimes more (Miles 2010), see Figure 4.5 for example of housing.

Dwellings were very much as Chadwick (1842) described above, as “the foci of disease”.

Figure 4.5 Market Court. A typical London slum in mid 1800s (Bentley 1971).

Subadult mortality was high in this cemetery; a survey of burial records between the years 1783 and 1798, records 40% of burials were under eighteen years, but the majority of those were under two years (66%). Recent research also suggests reduced survival in subadults compared to adults in this population (DeWitte et al. 2016). Diet was likely adequate in quantity, but not particularly nutritious, typically consisting of bread, potatoes, beer, and more rarely meat (Chadwick 1842). Rickets was a common pathology noted in this collection, particularly active lesions in infants, as well as evidence consistent with tuberculosis (Kausmally 2008). Of the samples selected for this thesis, St. Brides Lower – hereon referred to as Farringdon, represents the lowest

socioeconomic status group, who bore the brunt of the unsanitary and overcrowded living conditions that typified London poverty in this period.

These four socioeconomic groups represent some of the wealthier Londoners of the day as well as some of the poorest, but all who lived during a period of rapid social and economic change, characterised by increasing urbanisation, rural migration and disease. This was a period of increase: industry and trade boomed, general wages increased, food production rose dramatically due to the agricultural advances in crop production, and transport networks grew to connect all parts Britain (Landers 1993; Stearns 2012). This change, however, came with a cost to the population's health. The overcrowded city provided ideal conditions for endemic diseases such as tuberculosis, smallpox, measles, and typhus, while polluted waterways carrying cholera and typhoid. (Landers and Mouzas 1988; Landers 1993 Davenport et al. 2011). Within this context, the individuals analysed here should provide insight into how social factors might influence possible associations between childhood stressors and adult health outcomes.

4.3 Methods and approaches

4.3.1 The childhood environment: subadult stressors

Porotic lesions

Porotic hyperostosis are characteristic cranial lesions frequently associated with various anaemias (Stuart-Macadam 1985; Walker et al. 2009; Oxenham and Cavill 2010; Zariſa et al. 2016). On the crania, they occur primarily in the frontal, parietal and occipital bones or in the superior region of the orbits, known as cribra orbitalia. As this is predominantly a childhood condition, active outgrowth of trabecular structures are possible, but less likely in adults (Stuart-Macadam 1985; Sullivan 2005; Steyn et al.

2016), but quiescent lesions may still be observable and indicative of the condition experienced in childhood. All observable regions on the cranial vault and orbit roofs were inspected for lesions and recorded using Stuart-Macadam's (1991) criteria. This involves five stages from capillary like formations to active outgrowth in trabecular bone (Table 4.2). Porotic lesions on the vault were recorded separately to the orbits. Damaged areas were not scored.

Table 4.2 Five stages of cribra orbitalia (Stuart-Macadam 1991).

Score	Description	Image
1	Capillary-like formations etching the periosteum	
2	Scattered, fine foramina	
3	large and small isolated foramina	
4	Foramina have linked into a trabecular structure	
5	Outgrowth in trabecular form from the outer table surface	

Enamel hypoplasia

Defects of enamel hypoplasia are used in this research to indicate episodes of systemic stress that occurred during amelogenesis, resulting in defects visible on the crown surface. Impressions were taken of the teeth *in situ,* from which high definition replicas were later produced for recording the number and location of each defect. The processes involved in producing and imaging dental replicas as well as techniques used to identify and record defects are described below. Lastly, the ageing schedule used to establish the timing of defects as well as procedures to exclude worn crowns are described.

Dental impressions and casts

The maxillary central incisor and mandibular canines were selected for analysis as not only do these provide a register of defects from around one to six years of age, but as polar teeth they may be more sensitive to forming defects (Goodman and Armelagos 1985). Dental replicas were made of these crown, which is a two-step process. First, an impression of the specimen is made using a specialised silicone material then an epoxy replica is cast from this impression. The methods used in this study are based on standard procedures described in Hillson (1992). In preparation for making the dental impressions, all crowns were brushed to remove debris, and if necessary were wiped with a damp cloth. For application of impression material, loose teeth were positioned horizontally on a bed of modified paraffin wax so that their labial surface was uppermost. Some canines were not able to be removed from their sockets, and so the mandible was positioned such that the crown of interest lay horizontally. The

individual tooth crowns were covered with a fine body vinylpolysiloxane material (Take 1 Advanced ™, Kerr Corporation). This is a fast curing material that preserves detail down to ~ 1 µm. Once cured, the impressions were removed and numbered with their individual's identification number. Two types of replicas were made from the impressions. The first set were cast using epoxy resin (Buehler Epothin ™) following the manufacturer's instructions. This produced transparent replicas, the surface of which were analysed under a scanning electron microscope. The second set were cast in the same manner, but with the addition of gesso, an opaque white acrylic emulsion, which produced white opaque replicas – allowing defects to be easily visualised on macroscopic inspection. At all stages, impressions and casts were tagged with their respective identification numbers.

Recording defects

An important part of this research involves estimating the individual's age when each defect formed. Recording a defect's position as a percentage of original crown height provides a standardised approach allowing age to be estimated using ageing charts developed by Reid and Dean (2002). As age is determined by the defect's position, original crown height needs to be reliably estimated, a requirement that saw the development of a novel approach as part of this research and which is outlined in Appendix one. A two pronged approach to recording defects was used: the first stage required dividing the length of the crown into percentages of original crown height, or deciles, which was done on images where the crown surface is orthogonal to the lens to minimise foreshortening. This can make it difficult to detect defects as they are best visualised with an oblique light source, often requiring the angle between the crown and

the light source to be frequently altered. Therefore, the second stage involved defects being directly identified on the opaque replicas and the position of each defect cross referenced with the montage.

The clear epoxy casts were imaged under a scanning electron microscope (Jeol JCM-6000) using low magnification (15x – 25x). This entailed taking a series of images along the crown with the surface of the crown orthogonal to the lens, altering focal length as required. Each set of images were used to create a full montage of the crown in Inkscape (Free Software Foundation, Inc), on which a decile marked ruler could be extended from the original extent of the cusp to the cementoenamel junction (Figure 4.6). The original height of the crown, prior to any wear, was estimated for each crown using a regression equation specifically developed for this purpose. Its development and application is explained in Appendix one. Using the opaque replicas, defects were identified using low magnification (10x) and a movable LED light source. The most cuspal extent of each defect was recorded, as this marks the extent of crown formation completed when the stressor was experienced and to which an age estimate can be assigned. The position was recorded to the nearest 2.5% of original crown height, or 0.25 of a decile.

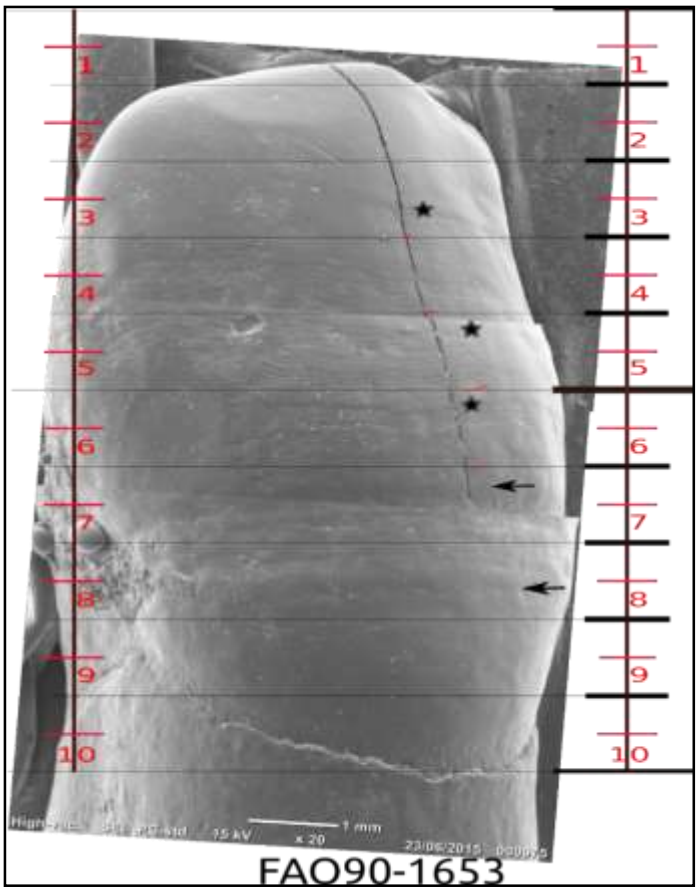

Figure 4.6 Montage of crown compiled from SEM images with decile marked rulers along each side. Arrows mark more defined linear grooves and asterisks mark fainter defects

Three types of hypoplastic defects were recorded including linear grooves, pits (either single or multiple), and plane type defects. In the field, the lowest level of linear defects to record is generally when a defect is palpable using either a fingertip or probe. This technique, however, has been suggested as too coarse and may miss more subtle but relevant defects (Hillson & Bond 1997; Hassett 2012, 2014). Studies using microscopic methods have demonstrated that higher resolution, which allows analysis of perikymata, permits finer grained information to be obtained (Hillson 1992; Hassett 2012, 2014; Cares Henriquez & Oxenham 2017). Due to the time consuming nature, however, and specialised equipment required for microscopic analysis (Hassett 2012), few studies have employed this methods and tend to be restricted to relatively small sample samples sizes (e.g., Hillson 1992; King et al. 2002; King et al. 2005; Hassett

2012; Cares Henriquez & Oxenham 2017), limiting the number of comparable studies. For these reasons, I chose to use a macroscopic method to identify hypoplastic defects in this research. This may mean that more subtle defects have been excluded form analysis. Defects were identified under magnification with an oblique light source and recorded if tactile. Some of these were subtle and not really apparent without magnification and oblique light, but were still discernable with a fingertip. Care was taken to ensure that prominent perikymata where not mistaken for hypoplastic defects, as suggested by Hillson (1996). This meant insuring that a defect represented a deficiency of enamel, such as a line or grove below the expected surface, rather than a raised ridge.

To differentiate between defects that are associated with systemic stressors and trauma, defects were tracked across all observable crowns (for example, canines and the central incisors), whenever possible. No dentitions were observed that suggested genetic defects. The central incisor was mainly used to help track defects. Originally, I hoped that earlier occurring defects, missed by the slightly later developing canines or when the canines were worn, might be able to be detected on them. However, in situations where the canines were worn the central incisor was as well. Although a few earlier occurring defects were detected - only very approximate age estimates could be assigned to them as original crown height could not be estimated for these teeth. Therefore I did not include these in my analyses. Defects were recorded on which ever canine had the least worn or abraded surface..

Defect timing

All age estimates are based on Reid and Dean's (2000) decile formation schedule (Figure 4.7). These ages were determined from histological assessments of

north European individuals, involving counts of striae of Retzius and periodicities for each individual. There are two things to note: first, these age estimations are not sex specific and females are thought to develop slightly ahead of males (Song and Goodman 1999). Second, possibly due to difficulties in obtaining age at enamel initiation for individuals, these estimations are based on a very small sample size that may not include encompass the full ranges of ages. Despite this, I believe these issues have only minor impact and unlikely to alter interpretations. Each decile of crown height was further divided into quarters and marked as either absent or present for a defect. No more than one defect was found to occur in any one quarter decile. Crowns which had damaged cervical enamel, where the cementoenamel junction was not observable were excluded (this only involved one crown). Deciles were then grouped into age ranges: 18 months up to 2 years, 2, 3, 4, and 5 years of age, and the number of defects occurring per age range reported for each individual.

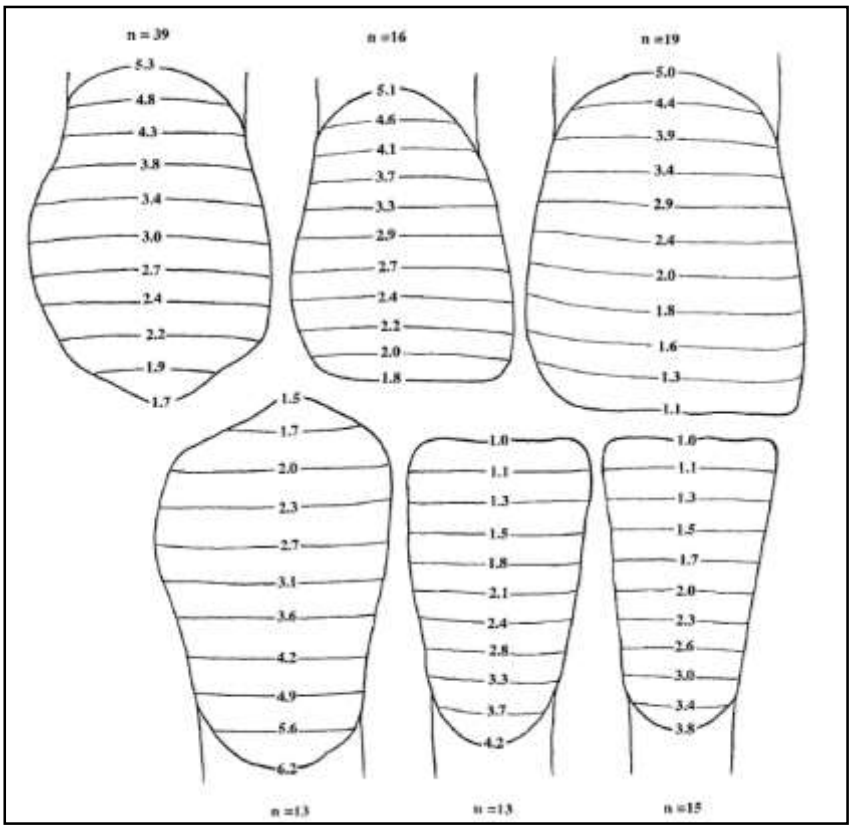

Figure 4.7 Timing of anterior tooth growth. Age is recorded in years at the completion of each decile (Reid and Dean 2000:138, Figure 1)

Selection of crowns based on wear

To minimise bias resulting from worn crowns, several criteria were used to allow a balance between maximum sample sizes and minimal bias that varies depending on the type of assessment. As shown in Table 4.3, enamel formed on the mandibular canine during the first six month period (from 1.5 years to 2.0 years) is most affected by crown wear. Due to the limited sample size this allows, I decided to start the analysis from two years of age, allowing full years to be assessed from that point onwards. For testing the effects of the total number of defects per individuals, only individuals with at least 80% of original crown height were included. This includes correlations between total hypoplastic defects and age at death, threshold effects, and annual regularity. Effectively, this means health insults experienced over four years, from the beginning

of the second year to the end of the fifth year of post natal life, are assessed. When testing the effects of defect timing, or the age of the individual when they experienced the causal health insults, two age ranges were affected: the second and third years following birth. For analysis of the second year, the exclusion of individuals with more than 20% of crown height worn (or 80% remaining) ensures only those with the full complement of enamel formed during this period is assessed. For defects formed during the third year of age, up to 50% of the crown can be missing before this year's enamel is impacted, which excluded only a single individual. Subsequent results will be reported based on the following ages, representing annual increments, when defects formed on the mandibular canine: two, three, four, and five years.

Table 4.3 Percentages of original crown height remaining (unworn) of mandibular canines and associated years observable by groups. Percentage of original crown height remain was quantified using the method described in Appendix one.

	n	Mean % worn	SD	Percentage of original crown height remaining					
				95% or more (from 1.6 years)		80% or more (from 2 years)		50% or more (from 3 years)	
				n	%	n	%	n	%
Male	103	18.8	1.18	17	16.5	66	64.1	102	99
Female	91	14.1	0.87	12	13.2	77	84.6	91	100
St. Bride's	41	14.5	0.89	7	17.1	34	82.9	41	100
Chelsea	59	15.9	0.97	7	11.9	44	74.6	59	100
St. Benet's	45	15.9	1.05	9	20.0	33	73.3	45	100
Farringdon	50	19.5	1.30	7	14.0	33	66.0	49	100
Total	195	16.5	1.07	30	15.4	144	73.8	194	99

Femur and tibia length

The maximum lengths of femora and tibiae were used to detect possible differences in lower limb length that might reflect environmental conditions, such as growth faltering, during development. A sample of thirty individuals were assessed and

measurements compared to those on the WORD database (2016). As the two sets of measurements were in agreement (see chapter five for interobserver error), WORD (2016) assessments were used for the remainder of the analysis. Measurements were assessed as described in Buikstra and Ubelaker (1994) using an osteometric board. Maximum femur length is the distance from the most superior point of the femoral head to the inferior edge of the distal condyles, while maximum tibial length is from the superior edge of the lateral condyle to the inferior tip of the medial malleolus (Buikstra and Ubelaker 1994). Damaged bones were not assessed unless the damage did not impact length measurements. If available, both left and right long bones were measured and mean values were used in analysis (to minimise possible impact of asymmetry). If only one side was available then this measurement was used.

4.3.2 Indicators of adult morbidity

Periosteal new bone formation

Periosteal new bone formation describes inflammation on the bone surface, specifically involving the periosteum, which responds to trauma or infection by forming new bone (Ortner 2003; Roberts and Manchester 2007; Weston 2012). When periosteal new bone is initially formed it appears as woven bone (porous, disorganised formation) indicating the lesion is unremodelled. Lamellar bone (smooth and organised) indicates the lesion was healed at the time of death, while a mix of the two states can suggest a chronic condition or a lesion in the process of healing (see Figure 4.8). Lesions were recorded by element, position, extent, and whether active, healed, or mixed.

Figure 4.8 Plaque like active periosteal new bone formation, left image. Smooth raised lesion of healed periosteal new bone, right image.

In addition to the tibia, which is most commonly recorded, I also checked the cranium, mandible, femur, and vertebral rib-ends and any occurrence of bilateral lesions were noted. My concern with only recording the tibia is that this bone is more susceptible to trauma as it is easily knocked and the bone is relatively unprotected by overlying soft tissue (Roberts and Manchester 2007). Therefore, differences in frequencies between the cemetery sites could possibly be influenced by activities as well as the type of clothing worn in life. Furthermore, my reason for recording periosteal new bone is not to compare frequencies with other populations, but assess variation within my selected samples. I suspect that extending the range of bones inspected will allow a more thorough assessment. As my sampling criteria ensured that all individuals had most relevant elements present (cranium, mandible, tibia, femur, and vertebral ribs-ends), bias due to missing elements should be minimal.

Periodontitis

Periodontal disease is used in this study as a marker of chronic oral bacterial infection, which may be associated with systemic diseases processes and have use as a skeletal stress indicator (DeWitte and Bekvalac 2010; Crespo et al. 2016). A recording scheme, developed by Kerr (1988), scores each interdental septum on the state of the bone, allowing the bony response to inflammation to be directly assessed. An advantage of Kerr's (1988) method is that it offers a solution to over estimations associated with methods that measure the height between the cementoenamel junction and the alveolar crest (Hillson 1996). A further advantage is that milder forms of periodontal disease (gingivitis) can be distinguished from more serious states (periodontitis), including severe forms identified by pocket type lesions (see Figure 4.9 for example).

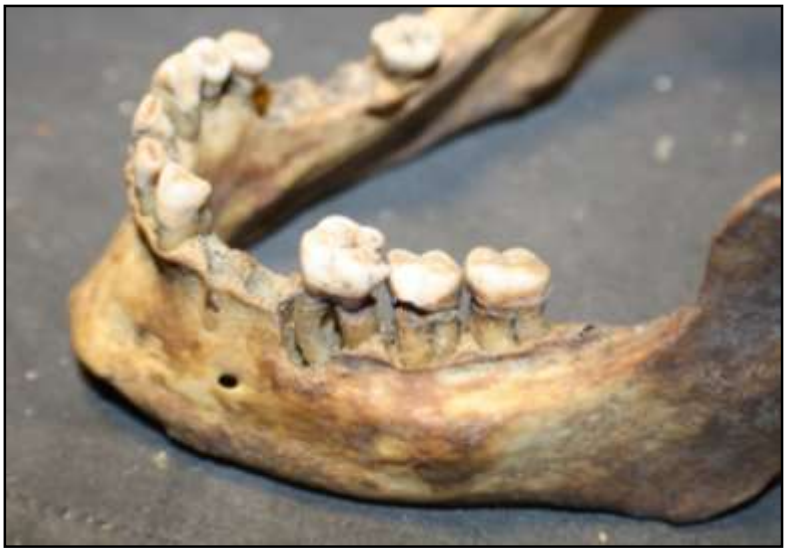

Figure 4.9 Mandible showing periodontitis; pockets are associated with M1 (score = 5) and M2, but not M3, which has horizontal bone loss (score 4). Interdental septa associated with the premolars show active outbreaks (score 3).

Kerr's (1988) scoring system is outlined in Table 4.4. Gingivitis is identified by the presence of bony reactions, such as pitting or groves, but where the original septum contour is still evident – once this architecture begins to break down it is considered

periodontitis. Kerr (1988) differentiates between active and quiescent states for general periodontitis outbreaks, while pocket lesions are describe by the amount of bone loss and may be either active or quiescent. Thus, based on porosity and architecture, each septa were scored 0 to 5 based on Kerr's (1988) classification system. Damaged septa or those associated with ante mortem tooth loss are not scored.

Table 4.4 Periodontitis scoring system. Based on Kerr (1988)

Score	Description	Implication
0	Unrecordable. Damage or ante mortem tooth loss	
1	Wall contour convex (incisors) grading to flat (molars). Cortical surface smooth and virtually no foramina or grooves	Healthy
2	Wall contour as above. Cortical surface shows many foramina and/or grooves. Occasionally gross interruption of cortex, but normal contour still maintained	Inflammation of overlying gingiva (gingivitis)
3	Breakdown of contour, with broad hollow or smaller areas of destruction. Lesions have sharp and ragged texture	Acute active bursts of periodontitis
4	Similar breakdown as above, but lesions have smooth surface with a porous or honeycomb effect.	Previously active periodontitis reverted to quiescent phase
5	Deep intrabony lesions (pockets) with $>45^0$ slope and depth > 3mm. May be sharp and ragged (active) or smooth and honeycomb (quiescent)	Severe[1] periodontitis, in either an active or quiescent phase.

1. While Kerr uses the term 'aggressive', I have chosen 'severe' to align with modern dental terminology where aggressive is reserved for a rare form predominantly afflicting adolescents.

Clinically, periodontitis is only diagnosed when actual alveolar bone destruction as occurred, as opposed to gingivitis where only the gingiva is affected. Therefore, for

purposes of analysis, scores of '1' (healthy septa) and '2' (gingivitis) are collapsed into a single group: absent for periodontitis. Likewise, quiescent and active lesions are grouped together, representing the more common chronic forms, while periodontal pockets (score =5), which represent the more severe condition are noted separately. Therefore, individuals are classified as either absent or present for periodontitis with any occurrences of pockets lesions noted. Individuals have potentially thirty scorable septa (if undamaged and without ante mortem tooth loss), so most present with a mix of various periodontitis states, or scores. Therefore, states are only considered as 'present' if they represent 25% or more of observable septa. This allows the more predominant conditions to be assessed for each individual. Individuals with less than five observable septa are excluded from analysis

4.3.3 Adult sex determination

Sex determination

Sex was estimated for a sample of 30 individuals and checked for agreement with estimates for the same individuals in the WORD database (2016). As the two sets of estimations corresponded well (see chapter five for interobserver error results), sex assignments in WORD (2016) were used for the reminder of the sample. General agreement was still assessed on a case by case basis, but scores were not recorded. Sex determination used methods outlined in Buikstra and Ubelaker (1994), including pelvic (Phenice 1969) and cranial traits. Specifically, cranial features included nuchal crest, mastoid process, supraorbital margin, supraorbital ridge/glabella, and mental eminence. Pelvic features included the ventral arc, subpubic concavity, ischiopubic ramus ridge, greater sciatic notch and preauricular sulcus. Estimations for each individual could

potentially be one of five states: 1 male, 2 probable male, 3 indeterminate, 4 probable female, or 5 female, for both cranial and pelvic traits. In situations where the two estimations differed, preference was given to the pelvic assessment as this is considered the more reliable (Buikstra and Ubelaker 1994). As my analyses required sex to be binary, those with a score of 2, 3, or 4, needed to be assigned to either male or female. Therefore, in ambiguous assignments, weight was given to the sub pubic traits, which are generally thought the more reliable (Buikstra and Ubelaker 1994). On this basis only one individual could not be assigned as either male or female, and was excluded from sex based analyses.

4.3.4 Age at death estimations

Overview of approach

A major aspect of my thesis involves comparing age at death of individuals who experienced different levels childhood stress episodes. This provides a basis for determining if, or when, earlier health deficits might impact adult health outcomes. Ageing adult skeletal remains, however, especially older individuals, is notoriously problematic (Bocquet-Appel & Masset 1982, Mays 2010; Falys and Lewis 2011). Therefore, after scoring skeletal traits indicative of age I used a Bayesian approach, described in Chamberlain (2006), to establish their association with known age using a sample of known age, St. Bride's crypt coffin plate collection. This collection had the name and age at death reported on lead coffin plates and is also one of the four skeletal samples used to address the main research questions in this thesis. In addition, the overall likelihood of death occurring at a certain age was provided by parish burial records that included both higher and lower status individuals buried in the parish, as

opposed to only the higher status coffin plate collection. This approach allowed the age trait scores for individuals from the other three samples, Chelsea, St. Benet's, and Farringdon, to be aligned with trait scores linked to known age in a different sample, but from the same time period. To further minimise ageing errors, age groups (20- 34, 35-49, 50-64, and 65 years and over) were used instead of more error prone point estimates. In addition to skeletal traits, I also investigated the usefulness of canine wear as a supporting criteria.

Skeletal Ageing traits

The most commonly used osteological ageing traits used in forensic and archaeological studies are the auricular surface and the pubic symphysis, followed by sternal ribs ends and cranial suture closure (review by Garvin and Passalacqua 2012). Age related changes to the auricular surface, as described by Lovejoy et al. (1985), and the Brooks and Suchey (1990) system for pubic symphysis ageing, were used in this research. In general, Lovejoy et al. (1985) assign scores that reflect age related changes to the articular surfaces, including billowing and striae, surface texture, porosity, exostoses, surface/margin break down, and changes to the apex and retro auricular regions as secondary characteristics. Brooks and Suchey (1990) propose six age phases that can be associated with a mean and 95% age range separately for males and females. This system tracks changes in surface billowing and ridges on the symphyseal face in conjunction with development of the ventral rampart and gradual erosion of surrounding rim or margin. Both these criteria are outlined in Buikstra and Ubelaker (1994).

Asymmetry between right and left scoring surfaces can be present at times, and is suggested to become more prominent with age (Overbury et al. 2009). Although some differences were evident in my samples, it was unusual for one side to be an entire score different to the other. In such situations, the older score was used, as suggested by Overbury et al. (2009). Damaged surfaces were not scored.

Dental wear also progresses with age and, in some populations, is sufficiently consistent to be used as an ageing technique (Brothwell 1981; Miles 1962, 2001). As it is strongly related to diet, there can be considerable variation in the degree of wear associated with age, especially between populations (Mays 2010; Buckberry 2015). As the amount of canine wear, or lost original crown height, had been quantified as part of this research, I investigated its usefulness in helping to assign, or support, age estimations. These dental and skeletal aging traits provided the raw scores on which Bayesian analysis was conducted.

Bayesian approach to ageing

Bayesian analysis allows additional information about the likelihood of an outcome to influence the calculated probability of the outcome occurring. In ageing skeletal remains this means that the probability of an individual being a certain age, given a specific trait score, can be calculated using the known likelihood of dying at a certain age. Bayes' theorem states that the final probability, known as the posterior probability, is equal to the prior probability of a trait score occurring, given a certain age, multiplied by the likelihood of an individual being that age.

The theorem can be written:

$$P(A|T) = \frac{P(T|A) \times P(A)}{\sum[P(T|A) \times P(A)]}$$

where P(A|T) is the posterior probability of age, given trait; P(T|A) is the likelihood, or conditional probability of a trait occurring at a given age, and P(A) is the prior probability of age – before any other information is considered (Gowland and Chamberlaine 2002).

The choice of an appropriate prior is a key aspect in Bayesian age estimations as it effectively provides weight to influence the posterior probabilities (Chamberlain 2006). I chose to use an informative prior derived from parish burial records, as suggested by Boldsen et al. (2002) and Chamberlain (2006). These data represented individuals buried in St. Bride's parish, including both high and lower socioeconomic groups. As this data was required before the transcription of all parish burials was completed, every burial for five two year periods were recorded and used instead (n= 1475). The selected biennial periods were 1783-1784, 1799-1800, 1811-1812, 1929-1830 and 1839-1840, which span most of the period to which the skeletal samples are dated and so should be representative.

Prior probability

Before Bayesian analysis could be applied to trait scores, the prior probabilities, P(A), of age at death needed to be determined. The prior is akin to a weighting factor that influences the likelihood of a trait being associated with a certain age at death by considering the probability of death occurring at that age. The age group specific

probability of death, calculated from life tables using parish burial data provided this. The mortality distribution based on burials for St. Bride's (n=1475) displayed a typical age at death pattern (Figure 4.10), suggesting they should provide an appropriate prior. High levels of mortality in the first years of life, followed by a decline that reaches a minimum in the early teens. Mortality begins to increase in early adulthood and peaks in the 60s age group before numbers start to decrease, reflecting the declining number of individuals still alive in the older groups. The informative prior is taken as the probability of death (q_x) obtained from mortality tables calculated using the burial data (Table 4.5).

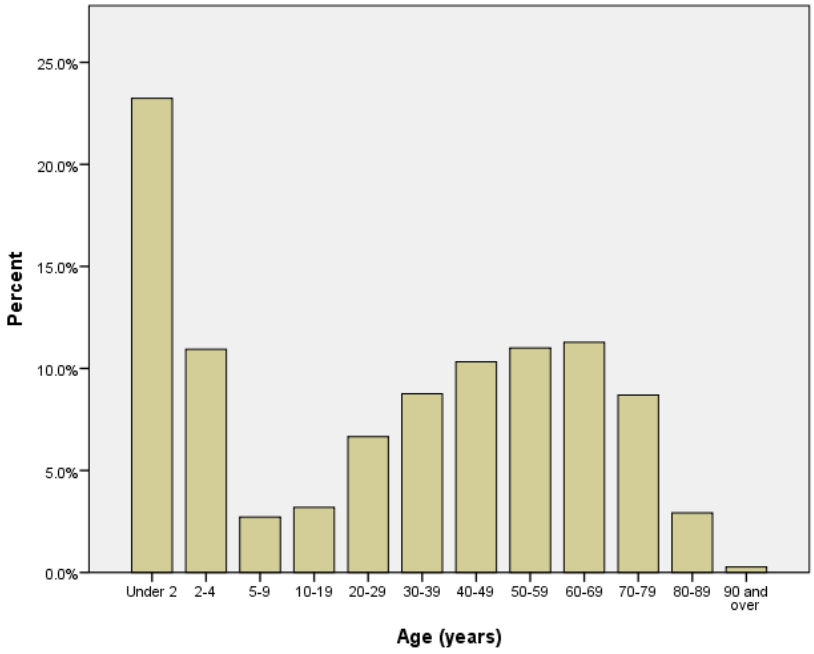

Figure 4.10 Age at death distributions from on parish records

Table 4.5 Life table calculated from St. Bride's burial records Bolded values are probability of death associated with each adult age group. x = age at start of interval, Lx = average years per person lived within age interval, Tx = sum of average years lived within current and remaining age intervals, l x = proportion surviving (survivorship), d x = proportion of deaths, q x = probability of death, e x = average years of life remaining (average life expectancy), n= number of deaths during interval.

x	l_x	d_x	$\mathbf{q_x}$	L_x	T_x	e_x	*n*
0-20	1.00	0.40	0.40	16.00	36.86	36.9	590
20-34	0.60	0.11	**0.18**	8.19	20.86	34.8	159
35-49	0.49	0.15	**0.30**	6.26	12.67	25.7	221
50-64	0.34	0.17	**0.50**	3.85	6.41	18.7	253
65+	0.17	0.17	**1.00**	2.56	2.56	15.0	252

Posterior probabilities

The steps involved with calculating posterior probability, as described by Gowland and Chamberlain (2002), are displayed in a series of contingency tables in Appendix two. Briefly this involves the distribution of trait scores with known age group, followed by the likelihood of a trait being associated with an age groups. The likelihood component, P(T|A), was determined using the high status individual from the St. Brides crypt sample (n=41), as known age at death could be associated with each trait score. Next, these values were multiplied by the prior probability from the life table probabilities of death, P(T|A) × P(A), which produces the overall probability of possessing a particular indicator state given the prior. The posterior probabilities were then calculated by dividing each probability of trait, given age, by the total portability for each score. These are displayed in Table 4.6

Table 4.6 Posterior probabilities of age, given trait, for the three ageing traits selected.

		Posterior Probabilities: Age, given trait. P(A|T)			
Trait	**Score**	**18-34**	**35-49**	**50-64**	**65+**
Auricular surface (Lovejoy et al. 1985)	1	0.00	0.00	0.00	0.00
	2	**1.00**	0.00	0.00	0.00
	3	**0.44**	**0.32**	**0.23**	0.00
	4	0.00	**0.58**	**0.42**	0.00
	5	0.00	**0.15**	**0.27**	**0.58**
	6	0.00	**0.32**	**0.68**	0.00
	7	0.00	0.00	**0.12**	**0.88**
	8	0.00	0.00	**1.00**	0.00
Pubic Symphysis (Suchey – Brooks)	1	**1.00**	0.00	0.00	0.00
	2	**1.00**	0.00	0.00	0.00
	3	0.00	**0.42**	**0.58**	0.00
	4	0.00	**1.00**	0.00	0.00
	5	0.00	**0.11**	**0.26**	**0.62**
	6	0.00	0.00	0.00	0.00
Canine Wear	1	**1.00**	0.00	0.00	0.00
	2	**0.20**	**0.37**	**0.24**	**0.18**
	3	0.00	**0.21**	**054**	**0.28**
	4	0.00	0.00	**0.28**	**0.71**

Correcting posterior probabilities

Several problems are evident in Table 4.6 that need to be addressed before the final probabilities can be applied to the other samples. First, there are scores to which

no probabilities are assigned because no individual in the reference sample displayed these scores. Second, there are unexpected gaps, such as where no individual in their 40s has an auricular surface score of '3', but it is associated with both older and younger individuals. Thirdly, the highest score '8' is only associated with the 50s age group, when it would be expected to also be found in the oldest groups. These issues are most likely symptomatic of the limited sample size; an ideal sample size would allow for the full range of ages associated with a given trait score to be realised. However, there are logical expectations that can be used to complete missing data, such as the lowest score should be found in the youngest age group.

Corrections to the final probabilities for auricular surface and pubic symphysis are displayed in Table 4.7. Explanations for each alteration is provided below the table. These include, for example, the addition of a probability value of 1.0 for an auricular surface score of '1'. This value is justified as it is a score that is normally only found in very young adults, but was absent in the reference sample, where only one individual was under 25 years. A score of '8' represents the oldest auricular surface age phase and so would be expected to be found in the oldest group, although not exclusively -as in the St. Brides sample it was evident in a 53 year old. This probability has been altered to reflect the expectation that it would be found in the oldest age group (probability 0.60), but also is still likely to occur in the 50-64 age group (probability 0.40). The only other probability of concern is the '5' score associated with the 65+ age group. To allow this to remain unchanged would mean a '5' score most likely indicates an older age than a '6' score. Simply exchanging this probability value with that associated with the same score, but for 50-64 age group, allows the weight to be moved to the younger group, but the range of possible groups is maintained. Although I suspect that with a

larger sample, a score of '6' would also be found in the oldest group, I am reluctant to alter probabilities too far.

Table 4.7 Corrected posterior probabilities for age, given trait, for the selected age traits.

		Corrected Posterior Probabilities: Age, given trait. P(A|T)			
Trait	Score	18-34	35-49	50-64	65+
Auricular surface (Lovejoy et al. 1985)	1	***1.00[1]***	0.00	0.00	0.00
	2	**1.00**	0.00	0.00	0.00
	3	**0.44**	**0.32**	**0.23**	0.00
	4	0.00	**0.58**	**0.42**	0.00
	5	0.00	**0.15**	***0.58[2]***	***0.27[2]***
	6	0.00	**0.32**	**0.68**	0.00
	7	0.00	0.00	**0.12**	**0.88**
	8	0.00	0.00	***0.40[3]***	***0.60[3]***
Pubic Symphysis (Suchey – Brooks)	1	**1.00**	0.00	0.00	0.00
	2	**1.00**	0.00	0.00	0.00
	3	0.00	***0.58[2]***	***0.42[2]***	0.00
	4	0.00	***0.40[3]***	***0.60[3]***	0.00
	5	0.00	**0.11**	**0.26**	**0.62**
	6	0.00	0.00	0.00	***1.00[1]***
Canine Wear	1	**1.00**	0.00	0.00	0.00
	2	**0.20**	**0.37**	**0.24**	**0.18**
	3	0.00	**0.21**	**054**	**0.28**
	4	0.00	0.00	**0.28**	**0.71**

Corrections

1 Probability added as no trait score available in ref. sample.

2 Probabilities switched to ensure logical age sequence.

3 Probability extended into next age groups to ensure logical age sequence.

Next, the final posterior probabilities are used to estimate the most likely age group each individual belonged to and back-tested against their known age group. If final age scores differ between the three traits, priority is given to the posterior probabilities associated with auricular surface scores. If this is absent then the pubic symphysis score is used. Canine wear scores are only used if the two standard traits are unavailable.

Back-testing assigned age groups

After each individual in the St. Brides samples was assigned to a probable age group, the age estimates were back-tested to assess the degree of accuracy and bias provided by the corrected posterior probabilities. While the probabilities of trait, given age, were derived from this sample, the posterior probabilities have been weighted by the mortality distribution derived from the parish records. In addition, the final set of posterior probabilities also include corrections done to ensure a logical sequence of age-trait relationships.

The frequency distribution of individuals assigned to estimated age groups and their known age groups are shown in figure 4.11. The most notable difference between the two distributions is the greater proportion of individuals estimated to be in the oldest age group. This is likely due to the informative prior used to calculate the posterior probabilities as this assume the greatest probability of death lies with the oldest group and so weighs the likelihood of death, and therefore, the probability of age at death, in that direction.

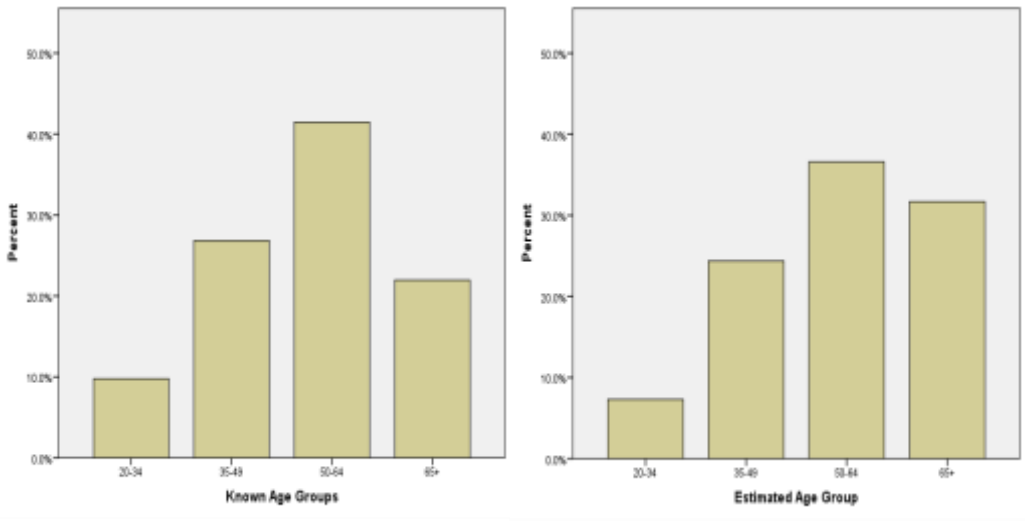

Figure 4.11 Age at death distributions of known age groups (left) and estimated age groups (right).

The percentage of individuals correctly assigned along with the difference between known and estimated age groups are plotted in Figure 4.12. The youngest and oldest age groups are the most accurately estimated, and therefore the most likely to be correctly identified. The two middle age groups are more concerning, with approximately half assigned to incorrectly. The majority of incorrect assignments are in an adjacent age group, although one individual was over estimated by two age groups. There is a general tendency for age to be over-estimated in the younger age groups and overestimated in the oldest two group.

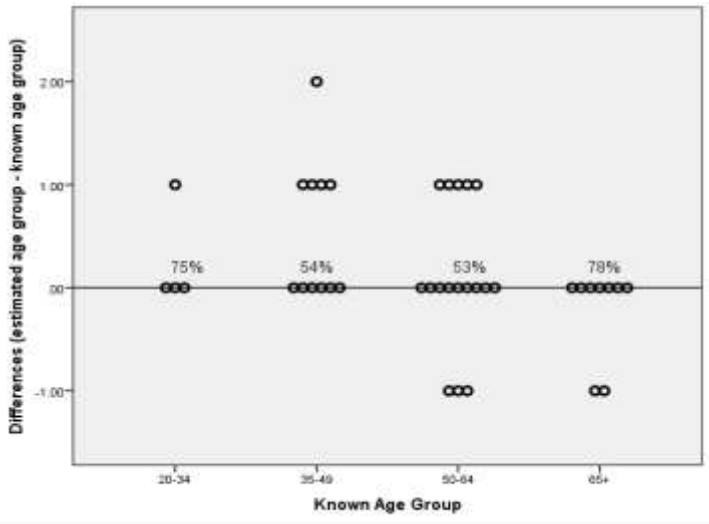

Figure 4.12 Differences between known age groups and estimated age groups using four age intervals.

Using the same approach as described above, final Bayesian posterior probabilities are applied to the traits scores of each individual, suggesting the most likely age group for each individual. The final distribution of age groups for each cemetery group by sex are displayed in Table 4.8.

Table 4.8 Distribution of individuals by age group determined using correct posterior probabilities, by sex for each cemetery sample.

Cemetery	Sex	Age group (years)								Total	
		20-34		35-49		50-64		65 & over			
		n	%	n	%	n	%	n	%	n	%
St. Bride's	Male	1	2.4	5	12.2	8	19.5	6	14.6	20	48.8
	Female	3	7.3	6	14.6	9	22.0	3	7.3	21	51.2
	Total	4	9.8	11	26.8	17	41.5	9	22.0	41	100.0
Chelsea	Male	4	6.8	6	10.2	12	20.3	8	13.6	30	50.8
	Female	11	18.6	3	5.1	11	18.6	4	6.8	29	49.2
	Total	15	25.4	9	15.3	23	39.0	12	20.3	59	100.0
St. Benet's	Male	3	6.7	6	13.3	17	37.8	3	6.7	29	64.4
	Female	5	11.1	3	6.7	7	15.6	1	2.2	16	35.6
	Total	8	17.8	9	20.0	24	53.3	4	8.9	45	100.0
Farringdon	Male	1	2.0	2	4.1	14	28.6	7	14.3	24	49.0
	Female	6	12.2	4	8.2	8	16.3	7	14.3	25	51.0
	Total	7	14.3	6	12.2	22	44.9	14	28.6	49	100.0
Total	Male	9	4.6	19	9.8	51	26.3	24	12.4	103	53.1
	Female	25	12.9	16	8.2	35	18.0	15	7.7	91	46.9
	Total	34	17.5	35	18.0	86	44.3	39	20.1	194	100.0

4.3.5 Parish Burial records

Skeletal data is supplemented by information from parish burial records, used to contextualise the socioeconomic groups. St. Bride's parish burial register records all internments within the church and upper ground as well as the lower ground. Of the

skeletal samples used in this research, the high socioeconomic status St. Bride's sample originates from the church internments while the lower socioeconomic status Farringdon sample is derived from the lower burial ground. Although these records directly reflect only two of the skeletal samples, they represent the two most extreme social classes. The relatively more middling samples, Chelsea and St. Benet's, should therefore be expected to fall within these extents. Figure 4.13 shows a page from St. Bride's burial registry.

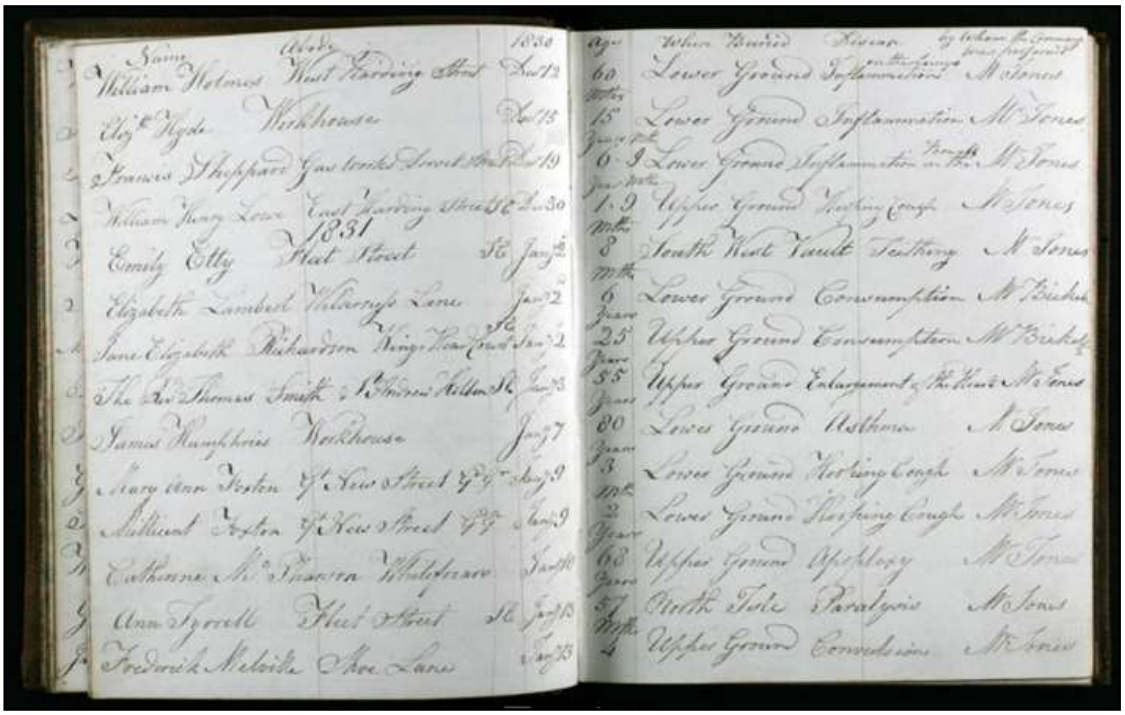

Figure 4.13 Example of a page from the St. Bride's burial register.

These burial records have been digitised and are available through subscription to the genealogy website www.ancestry.com. Prior to 1783, records became increasingly illegible, but all burials between 1783 and 1853 were transcribed into a spreadsheet, totalling 9239 individuals. The burial crypts were closed in 1852 by an act of parliament after a cholera outbreak and concern with the overcrowded nature of many burial grounds (personal communication with Dr Rebecca Redfern, Museum of

London curator). Although a few burials (n=21), presumably in family vaults and plots, took place until 1853, none were buried in the lower ground after 1849. Name, address, age, sex (based on first names of which 81 were ambiguous and unable to be assigned), and cause of death were recorded. Cause of death was not reported consistently throughout this time, with 13% of causes being either unrecorded or illegible.

Recorded causes of death

Reported causes of death are often problematic (see Alter and Carmichael 1999). In many cases the reported cause of death is little more than a description of the most obvious symptom, such as 'fever', or the affected region - 'affliction of the head,' or even the circumstances seemingly associated with the death, which may or may not be relevant, for example, "ate a great quantity of peaches". However, some causes are more reliable as people at the time were acutely familiar with their symptoms and progression, such as smallpox (Landers 1986; Alter and Carmichael 1999). The virulent smallpox virus (*Variola major*) is spread via inhalation of respiratory droplets (Riedel 2005). The characteristic blisters associated with the smallpox virus (Variola major), developed into hard or 'shot-like' lesions clearly distinguishing it from measles, chickenpox, or secondary syphilis. Furthermore, the rash spread over the body in a centrifugal pattern with the face, hands, and feet most affected, see Figure 4.14 (Fenner et al. 1988). For those who survived the infection, lifelong immunity was acquired. Smallpox is considered one of the most reliable causes of death reported in the London bills of mortality (Lander's 1986; Davenport et al. 2011).

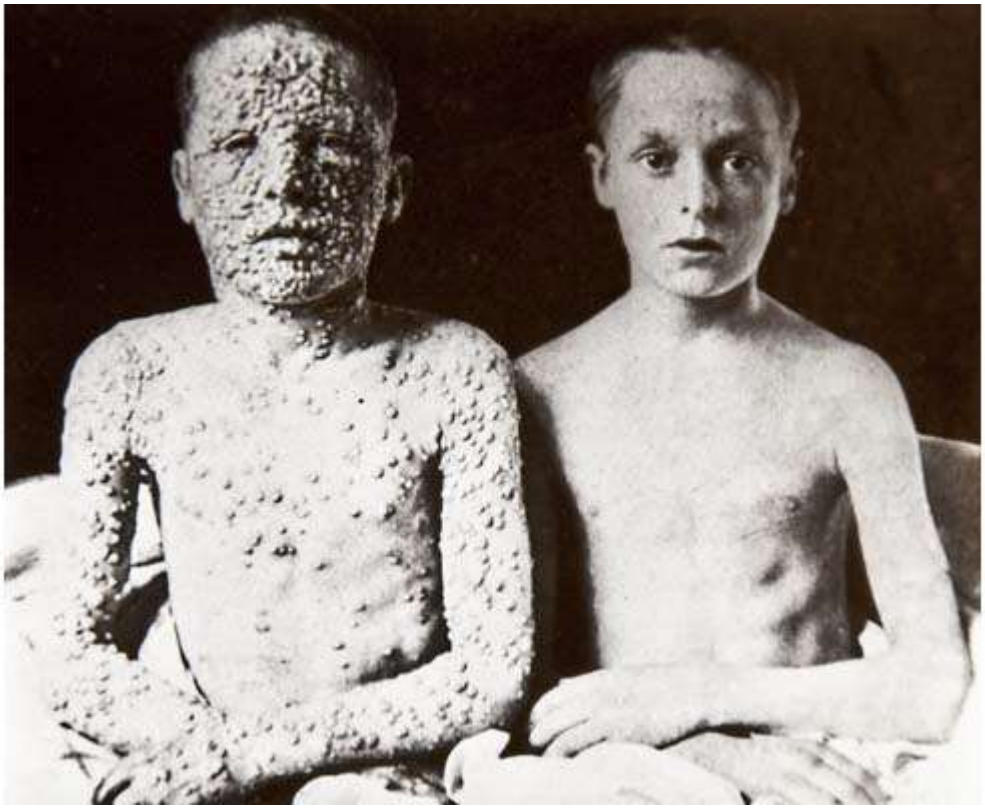

Figure 4.14 Two boys with smallpox. The rash on the boy on the right is at the earlier macular stage, while the boy on the left is at a later stage with vesicles – the potential for facial and corneal scarring is apparent (Wikimedia commons).

Burials attributed to cholera (*Vibrio cholera*) and tuberculosis (*Mycobacterium tuberculosis)* may be somewhat less reliable. The cholera bacterium is contracted through contaminated water and food, frequently associated with unsanitary conditions where faecal material is present in water supplies (Glass and Black 1992). Initial exposure to the pathogen induces immunity that may lessen the severity of subsequent infections (Glass and Black 1992). The most obvious symptoms of cholera is the excessive amounts of 'rice water' diarrhea, and severe dehydration (Sack et al. 2004). However, it is possible that in the burial records, other types of diarrheal diseases may have mistaken for cholera and vice versa (Barua 1992). Other diseases are likely to be underestimated, particularly tuberculosis. Pulmonary tuberculosis, then referred to as consumption, was well known, but as not all victims display expected symptoms it may

not always have been recognised (Alter and Carmichael 1999). A common transmission rout of infection is through inhalation of bacilli, but *Mycobacterium bovis* can be contracted through consumption of contaminated milk (Cruz and Starke 2007). Extrapulmonary infections were often known by other names, such as Potts disease, referring to a vertebral foci of infection (Daniel 2006). Many causes referred to in the burial records as decline, phthisis, or simply 'wasting disease' are likely to have been tuberculosis (Frith 2014). Despite these concerns, causes of death can still provide useful information, demonstrating, for example, how some diseases may differentially impact socioeconomic groups. In addition, due to the lifelong immunity smallpox confers, can be a marker of migrants, particularly adults who originated from rural regions with low or spasmodic infections rates (Landers 1993; Davenport et al. 2011). Adult burials attributed to either tuberculosis (consumption), cholera, or smallpox are extracted for analysis focusing on the variable risks of death amongst adult age groups, sex, and socioeconomic status.

Known age at death and mortality risks

Additional information provided by burial records that is particularly useful is age at death. This information is used to calculate an informative prior, used in a Bayesian aging approach for the skeletal material. In addition, the detailed and relatively accurate mortality distributions are used to investigate how mortality risks differed between the sexes and amongst the socioeconomic classes. Although, recorded age is still error prone, in the majority of cases it is unlikely to be inaccurate by more than a few years for adults and considerable less for children. I checked this with a sample of 15 individuals for whom both baptism and burial records had already been

matched. Their reported age was subtracted from the year of death and compared to their baptism date. Of these 15 individuals, there were four whose year of birth was in error by one year, while all the others in the sample matched. Baptisms were often months, sometimes years after the birth, particularly when a number of children in one family were baptised at the same time (as evidenced in the parish baptism records), so it is likely that the ages at death were in fact correct. Although this is only a small sample, and it would certainly be worthwhile to perform a larger analysis, it suggests at the very least that recorded age at death is considerably more accurate than skeletal estimations of age.

4.3.6 Inter and intraobserver error study

The degree of inter and intraobserver error that might exist between my assessments and those of other observers was tested over various skeletal and dental traits. This was to ensure that measurements used in this research, but which were recorded by other observers, such as femoral and tibial lengths are in accord with measurements I myself would take. Trait scores, particularly pelvic ageing scores can be quite subjective, so it was important to check that my assessments are similar to those of other observers. As this research relies on assessments of hypoplastic defects in terms of crown height deciles and associated ages, these are also tested for interobserver error.

Prior to accessing data on the WORD database (2016), interobserver error was tested on thirty eight individuals, although not all traits were observable on all individuals. These comprised of individuals recorded during the second week of recording during my first visit to the museum. The auricular surface (Lovejoy et al.

1985), pubic symphysis (Brooks and Suchey 1990), and sex designation based on standard cranial and pelvic traits (Phenice 1969; Acsadi and Nemeskeri 1970), were all recorded. In addition, maximum length of left femora and tibiae were measured on an osteometric board and recorded in millimetres. These assessments were then checked for reliability against assessments recorded on the WORD database (2016) by experienced osteologists at the Museum of London.

To test intra observer error in recording hypoplastic defects, I rescored a complete cemetery sample (Chelsea Old Church, n = 55) approximately six months after my main recording session. At the same time, another observer (CBS) who was blind to my assessments also scored crowns from another sample (St. Benet's, n=20) so inter observer error could be assessed.

Interobserver error: skeletal trait scores, sex, and long bone measurements

Cohen's kappa was run to determine the agreement between auricular surface and pubic symphysis scores recorded by myself and osteologists at the Museum of London. There was reasonable agreement for both sets of scores: auricular surface (n=33), $\kappa = 0.646$, 95% CI (0.462 – 0.830), $p < .001$; pubic symphysis (n=26), $\kappa = 0.674$, 95% CI (0.447 – 0.901), $p < 0.001$. Cohen's κ above 0.80 reflects a strong level of agreement, while between 0.60 and 0.79 is considered moderate; these results reflect the subjective nature of these scoring systems (McHugh 2012). Cohen's κ for sex assignment showed very good agreement (n=38), $\kappa = 0.844$, 95% CI (0.709 – 0.979), $p < 0.001$, demonstrating the more reliable nature of these assessments. Femoral and tibial measurements were assessed collectively and a strong correlation is evident between the two sets of measurements: Pearson's $r = 0.99$, $n = 40$, $p<0.001$. This

suggests the long bone lengths measurements already recorded by Museum of London osteologists would not differ significantly to my own.

Intraobserver error: hypoplastic defects

A strong Pearson's correlation was found for total defect numbers, per individual, for the two sets of recordings ($R = 0.82$, $p < 0.001$, $n= 55$). In general, more defects were recorded in the second assessment possibly reflected the subjective nature of the lowest level to record. Some faint defects were detected under oblique light and magnification, but were questionable to discern by touch.

Next, error associated with the presence or absence of defects per age (years) and deciles is checked as these are the basis for much of the analyses undertaken in this research. When defects were assessed by age in years, Cohen's kappa suggest a strong level of agreement: $\kappa = 0.879$, 95% CI (0.822 – 0.936), $p < 0.001$, n=275. Similar results are returned for deciles: $\kappa = 0.705$, 95% CI (0.640 – 0.770), $p <0 .001$, n=275. Overall, the intra observer error is reduced when defects are analysed in terms of age, as there are fewer groups (i.e. five) compared to deciles (i.e. ten). This is likely because when defects lie close to a decile division, determining which decile the defects occlusal edge is situated in can be difficult, especially as the occlusal defect edge is often more subtle than the cervical border.

Interobserver error: hypoplastic defects

Pearson's Product Moment correlation for the total number of defects between myself and a second observer (CBS) suggests reasonable agreement between total number of defects recorded (Pearson's $R = 0.774$, $n = 20$, $p < 0.001$). Most error is due

to total defects counts varying by one defect, but there is a slight tendency for the second observer (CBS) to record more defects (Figure 4.15). This most likely reflects issues surrounding the lowest level to record, as determining if a defect is actually perceptible with a fingertip is relatively subjective.

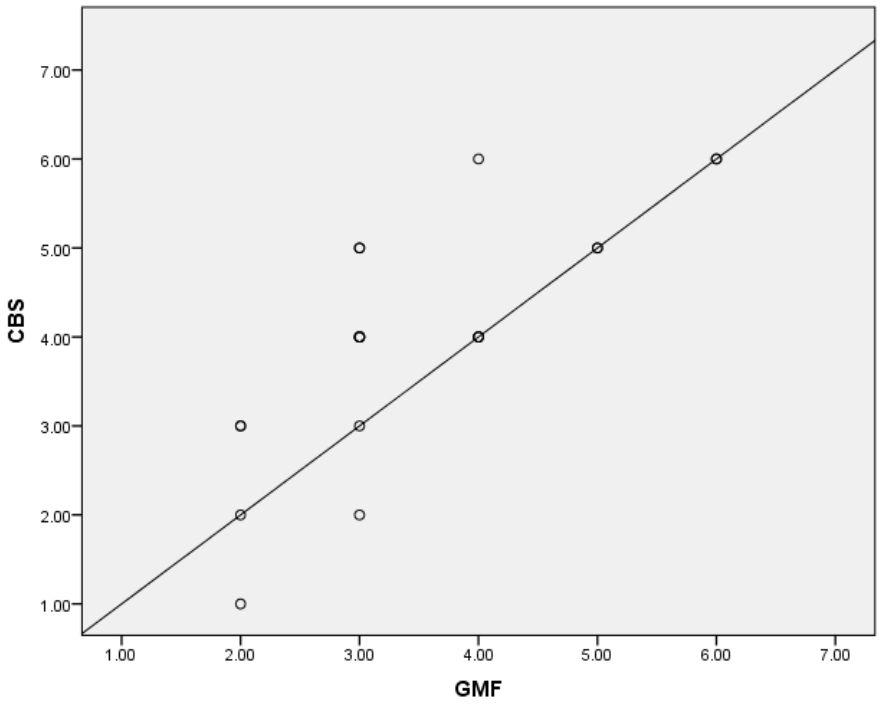

Figure 4.15 Scatter plot showing corresponding numbers of defects recorded by myself (GMC) and another observer (CBS) on 20 canine crowns. Bolded circles represent multiple values (n= 20).

When number of defects were grouped by age at formation, from 1.5 to 6 years, Cohen's kappa suggest a good level of agreement between the two set of observations: $\kappa = 0.632$, 95% CI (0.497 – 0.767), $p < 0.001$, n=92. Observer agreement was slightly strengthen when the presence or absence of defects occurring in each age group were assessed: $\kappa = 0.689$, 95% CI (0.542 – 0.836), $p < 0.001$, n=92. This variation again highlights the subjectivity of determining if faint defects are actually tactile.

Although some degree of error between measurements, and observers, is inevitable, most assessments here were in good agreement. The most concerning are

ageing traits scores for the auricular surface and pubic symphysis, which are known to be problematic (Falys and Lewis 2011). The interobserver error reported here is not exceptional (see Merritt 2014). For example, a similar level of agreement ($\kappa = 0.66$) was reported for auricular surface scores between various observers (number was not supplied) in Buckberry and Chamberlain (2002:235) and suggested to reflect a low level of interobserver error. The subjective nature of determining the lowest level of hypoplastic defect to record is an issue that researchers have attempted to resolve using engineering microscopes (Hillson and Jones 1989; Hassett 2012), but which are not available to all researchers. The differences reported here, however, were relatively minor and suggest that results reported by other researchers on occurrences of enamel hypoplasia would still be comparable.

4.3.6 General statistical approaches

Several different statistical approaches are used in this research. An overview of survival analysis and risk assessments is provided first, which concerns much of the main analyses. I discuss then how I propose to deal with hypothesis testing and multiple comparisons. All statistical analyses are undertaken using IBM SPSS (version 20).

Survival and relative risk analysis

Associations between childhood stress indicators and adult mortality and morbidity (periodontitis and periosteal new bone) is tested using two approaches. First, Kaplan-Meier survival analysis is used to understand possible differential impacts on mortality over all adult age groups. Relative risk assessments are then used to assess the likelihood of surviving specifically past 35, 50, and 65 years as well as risks associated

with morbidities. For example, is there a significantly increased risk of periodontitis if an individual had annually occurring hypoplastic defects between two and six years of age? Or did they have an increased risk of dying prior to 35 years of age if they had more than three defects between two and six years of age?

Kaplan-Meier analysis is a non-parametric method used to generate separate cumulative survival curves, calculated for each group, which allows the probability of surviving past a certain age to be established (Zwiener et al. 2011). Log-Rank tests are used to determine if Kaplan-Meier curves are significantly different, however, this does assume that the risk of death is proportional across all age groups. If the hazard is not proportional, for example if there is a greater risk in one age group compared to others, it may not detect this as significant. In this research, mortality risks are considered for four broad age ranges that span adulthood: 20-34, 35-49, 50-64, and 65 years and over. Therefore, the risk of death may vary by age group, meaning the hazard of death may not be proportional. To investigate this likelihood, the relative risk of dying before or after 35 and 50 years will be used to detect risks that might not be present equally over all of adulthood.

Risk ratios are also used to assess relationships between childhood stress indicators and adult morbidities. Relative risk analysis assesses the differential risk of an event, such as death, occurring before or after a point in time, given the presence or absence of certain conditions, such as hypoplastic defects. The risk ratios describe the difference in magnitude of risks between individuals with and without the specific condition. For example, the relative risk ratio of dying after a certain age, describes the difference in risks for those with hypoplastic defects relative to those without defects. In general, these assessments entail construction of 2x2 contingency tables, where the likelihood of a random effect will first be established using Chi square tests. If cell

values are significantly different to those expected by chance, then risk ratios between those with and without the condition are sought. Significance for the risks are then based on their 95% confidence intervals, which must not include '1' to be significant. As this two stage method is already conservative in its approach to testing, a Bonferroni adjustment, discussed next, was not applied. Other than the confidence intervals used for risk analysis, statistical significance is determined through hypothesis testing.

Statistical significance

Much of the statistical analysis in this research involves multiple comparisons, which can present problems when a conventional alpha level ($\alpha = 0.05$) is used. For example, if one is testing a number of variables, the chance of erroneously rejecting a true null is increased; twenty tests would mean that instead of making one type I error, one is more likely to make ~12 (0.95^{20}=0.4 or 60% of the time) (Bland and Altman 1995). The Bonferroni adjustment offers a way to address this by dividing the alpha level by the number of tests so that when considered as a whole, the probability of making a type I error 5% of the time is maintained (Bland and Altman 1995). The Bonferroni adjustment is calculated thus:

$$P_i \leq \frac{\alpha}{N}$$

where P_1 is the adjusted probability level, α is the significance level and N is the number of tests.

Although in many situations an adjustment is very appropriate, it is considered conservative. Therefore, although one is less likely to commit a type I error, the likelihood in committing a type II error can become unreasonably high (Rothman

1990). Another relevant criticism of the Bonferroni adjustment is that whether a result is deemed significant or not is largely determined by the number of tests involved, which means interpretation and research findings are also driven by the number of tests (Perneger 1998). A further issue is when relatively small samples sizes are used, such as in this research, because statistical power is influenced by sample size. Statistic power, or the ability to reject a false null hypothesis, is determined by three main factors: the significance level chosen, the size of the effect in the population, and sample size (Perneger 1998). Therefore with small samples, not only is it relatively difficult to detect a real effect in the data, but also more difficult to obtain very small probability values. As the Bonferroni adjustment does not consider sample size – only the number of tests, the ability to detect a true effect when it is present is reduced even further. One approach statisticians suggest is that all probability values should be reported, but discussed in light of expectations as well as reasons for the specific test (Rothman 1990; Perneger 1998).

For this research, I report all probability values below 0.05 alpha level, but place greater importance on values that fall below a Bonferroni adjusted alpha level. When testing effects for each of the four age at death groups or the four cemetery groups, an alpha level of 0.012 is assumed, which equates to a standard level (frequently used in anthropology) divided by the number of tests (α=0.050/4). However, results which return probability values below α=0.050 are still reported as suggestive. When relative risk ratios are assessed, this approach was not applied. For risk ratios to be deemed statistically significant, frequencies must first be found to vary significantly from a random distribution using a Chi square goodness of fit test (α= 0.05), then the ratios must also significantly vary between exposed and unexposed for any condition using effectively the same criterion. To apply a Bonferroni adjustment as well would be

excessively conservative. In Chi square tests where the expected cell counts are less than five, a Fisher's exact test is used to provide an exact probability value. In situations where the contingency tables exceed 2x2 (rows and columns), the Freeman-Halton extension to Fisher's exact test is used. All subsequent results will be reported separately for males, females, and for each cemetery sample, which represent differing socioeconomic groups: High status St. Bride's, middle to high status Chelsea, middle status St. Benet's, and low status Farringdon.

CHAPTER FIVE: CHILDHOOD ENVIROMENT RESULTS

5.1 Childhood environments through adult indicators

Environmental conditions experienced in infancy and childhood are strongly connected to an individual's risk of exposure to stressors during this period as well as their ability to recover. Therefore, it is useful to try and understand how environments may have varied between socioeconomic groups. In addition, as my skeletal samples are all adults, they represent only individuals who survived earlier stressors and may therefore represent a biased subsample. Because direct and indirect mechanisms operating across the life course, such as scarring and selective mortality, can shape adult age at death profiles, understanding which mechanisms might be operating during childhood can help untangle seemingly paradoxical outcomes sometimes connected to adult mortality. Information on the various conditions the adults in my samples may have been exposed to as children is therefore particularly important to understanding life course connections regarding health. Childhood health experiences that might differ by sex are explored first followed by the four cemetery samples representing groups of varying socioeconomic status.

Cribra orbitalia and porotic hyperostosis are possibly the earliest stress indicators recorded in this research and are analysed first followed by enamel hypoplasia that reflect stressors between two and six years. Femoral and tibial length may reflect chronic growth deficits operating at different times over subadult years and are assessed last in the series. Data derived from burial records for the high and low socioeconomic groups (St. Bride's and Farringdon) allows mortality risks experienced by infants and children of markedly divergent social groups to be investigated. Using

these data, I attempt to characterise the early environments that adult survivors may have experienced. The chapters following this will report results pertaining to the adult environments, followed by associations between childhood and adult health outcomes at the individual level.

5.2 Indicators of childhood environment

5.2.1 Cribra orbitalia and porotic hyperostosis

Frequencies of the various states of cribra orbitalia and porotic hyperostosis per group are presented in Table 5.1. Porotic hyperostosis was nearly absent, with only three individuals (7%) from St. Benet's with cranial vault lesions. Therefore other than noting its presence in the one group, no further analyses are undertaken. Cribra orbitalia was found in all samples, with just under a third of all individuals exhibiting lesions of some stage, however, no individual had outgrowth of cribrotic lesions (score = 5).

Table 5.1 Frequencies and counts (N) for cribra orbitalia and porotic hyperostosis by group.

Group	% Cribra orbitalia scores						% Porotic Hyperostosis	
	N	0	1	2	3	4	Present	N	Present
Male	89	68.5	13.5	7.9	7.9	2.2	31.5	99	2.0
Female	91	74.7	9.6	3.6	6.0	6.0	25.3	86	1.2
St. Bride's	41	86.8	7.9	2.6	2.6	0.0	13.2	40	0.0
Chelsea	48	72.9	8.3	8.3	8.3	2.1	27.1	53	0.0
St. Benet's	39	51.3	17.9	12.8	12.8	5.1	48.7	43	7.0
Farringdon	48	72.9	12.5	2.1	4.2	8.3	27.1	50	0.0

While females have a slightly lower crude prevalence of cribra orbitalia than males, this difference is not significant ($X^2 = 0.80$, df =1, p = 0.402). Females and males do not differ significantly by lesion state, either (Fisher-Freeman-Halton exact p =

0.455). The relatively high frequency of individuals with no discernible lesions do not bias these outcomes. When only individuals with lesions were considered, the likelihood of any particular lesion score did not differ significantly by sex (Fisher-Freeman-Halton exact, p = 0.404).

Among the cemetery groups, St. Benet's has the highest frequency of cribrotic lesions present, while St. Bride's reports the lowest. Differences among the four cemetery groups are statistically significant (X^2 = 12.191, df = 3, p = 0.006). In this test, the standardised residues show a greater than expected occurrence of lesions for middle status St. Benet's individuals and fewer than expected in high status St. Bride's, revealing that these two groups are responsible for the significant probability value (Table 5.2). Middle to high status Chelsea and lower status Farringdon have similar lesion frequencies, neither group's frequencies deviating from those expected given total frequencies. Although the frequencies of individuals with cribra orbitalia differ significantly between cemetery groups, the distribution of lesion scores does not (Fisher-Freeman-Halton exact, p =0.096). This was also the case when only individuals with cribrotic lesions were considered (Fisher-Freeman-Halton exact, p = 0.714).

Table 5.2 Contingency table showing frequencies for the presence and absence of cribra orbitalia amongst the cemetery groups. Bolded standard residual denote values nearing or over 2.0 (+or-), which suggest values most responsible for significant probability value.

		Cribra orbitalia	
		Absent	Present
St. Bride's	% within Cemetery	86.8%	13.2%
	Count	33	5
	Std. Residual	1.2	**-1.8**
Chelsea	% within Cemetery	72.9%	27.1%
	Count	35	13
	Std. Residual	0.1	-0.2
St. Benet's	% within Cemetery	51.3%	48.7%
	Count	20	19
	Std. Residual	-1.5	**2.3**
Farringdon	% within Cemetery	72.9%	27.1%
	Count	35	13
	Std. Residual	0.1	-0.2

5.2.2 Enamel hypoplasia

Enamel hypoplasia, an important tool in characterising early environments, is ubiquitous in these skeletal samples; very few people escaped childhood stressors that resulted in defects (Table 5.3). While the percentage of females with defects does not differ significantly to males ($X^2 = 1.930$, df = 1, p = 0.165), females did have significantly fewer defects per individual than males (mean Δ = -0.44, t = 2.268, df =141, p = 0.025). Across cemetery groups, neither the frequencies of individuals with hypoplastic defects (Fisher-Freemman-Halton exact, p = 0.368) nor the number of defects per individual (F = 1.014, df = 3, p = 0.389) differed significantly. Most defects are linear type with only five individuals exhibiting pit or plane type defects. These five

defects, which were present on antimeres, are included in analysis. Overall, the average number of defects was two per individual.

Table 5.3 Percentage of individuals with enamel hypoplasia (EH) and mean number of EH per individual (P.I.). SD= standard deviation. SES= socioeconomic status. Analysis only includes individuals with canines that have at least 80% of original crown height remaining (n=161). Sex for one individual was not determinable.

Group	SES	N	% with EH	Mean P.I. (SD)
Male		66	92.4	2.24 (1.26)
Female		77	87.0	1.80 (1.09)
St. Brides	High	34	97.1	2.12 (1.09)
Chelsea	High/middle	44	88.6	1.79 (1.05)
St. Benet's	Middle	33	87.9	2.24 (1.35)
Farringdon	Low	33	84.8	1.94 (1.19)
Total		144	89.6	2.02 (1.17)

5.2.3 Femoral and tibial lengths of adults

Mean femoral and tibial lengths are displayed in Table 5.4, including the number of observable elements. As expected, males have longer leg bones on average than females: femur length mean difference = 29.26 mm, SD = 4.42; tibia length mean difference = 28.71 mm, SD = 3.87. These mean values were then used to calculate sex specific Z scores.

Table 5.4 Mean lengths of femora and tibiae by sex. SD = standard deviation

Sex	n	Element	n	Mean (mm)	SD
Males	54	Femur	54	448.86	25.53
		Tibia	54	362.74	21.99
Females	64	Femur	64	419.79	22.49
		Tibia	54	334.03	18.01

Femoral and tibial lengths and standardised Z scores are displayed in Table 5.5 for each cemetery group. These differ only slightly, with ANOVA detecting no significant differences in the femoral and tibial Z scores among cemeteries for the whole group ($p \geq 0.212$) or when males ($p \geq 0.285$) or females ($p \geq 0.162$), are considered separately.

Table 5.5 Femoral (upper section) and tibial (lower section) lengths by cemetery group and sex, including actual means in millimetres (mm) and standardised Z scores. SD = standard deviation.

Element	Cemetery	Group	n	Mean (mm)	SD	Mean (Z score)	SD
Femur	St. Bride's	Male	16	455.28	26.60	0.25	1.04
		Female	17	418.44	26.67	-0.06	1.18
		Total	33	436.30	32.20	0.09	1.11
	Chelsea	Male	17	446.85	22.75	-0.08	0.89
		Female	20	428.85	17.29	0.40	0.79
		Total	37	437.12	21.69	0.18	0.85
	St. Benet's	Male	6	459.17	20.88	0.40	0.82
		Female	8	413.94	15.82	-0.26	0.70
		Total	14	433.32	29.01	0.02	0.80
	Farringdon	Male	15	440.17	27.99	-0.34	1.10
		Female	19	413.95	24.11	-0.26	1.07
		Total	34	425.51	28.07	-0.30	1.07
Tibia	St. Bride's	Male	14	366.78	23.58	0.18	1.07
		Female	17	334.29	17.97	0.01	1.00
		Total	31	348.97	26.14	0.09	1.02
	Chelsea	Male	13	359.96	20.22	-0.13	0.91
		Female	15	333.53	19.24	-0.03	1.07
		Total	28	345.80	23.53	-0.07	0.98
	St. Benet's	Male	14	363.25	16.62	0.02	0.75
		Female	9	324.22	10.56	-0.54	0.76
		Total	23	347.98	24.15	-0.20	0.74
	Farringdon	Male	13	360.61	28.16	-0.10	1.28
		Female	13	341.04	19.23	0.39	1.07
		Total	26	350.83	25.64	0.15	1.18

5.2.4 Childhood indicators in adult survivors

Overall, the frequencies of stress indicators were not extremely varied between the sexes or amongst the socioeconomic groups, but differences were present. The crude prevalence of cribra orbitalia was similar between males and females, but females did have, on average, slightly fewer hypoplastic defects than males, while the percentage of affected individuals did not differ. The higher status group, St. Bride's, has generally fewer and milder occurrences of cribra orbitalia, while middle status St. Benet's has the highest crude prevalence of lesions. In addition they are the only sample to have porotic hyperostosis. Enamel hypoplasia was common in all socioeconomic groups, with no particular variation amongst the groups in either the percentage of individuals affected or the average number of defects per individual. Femoral and tibial lengths showed no significant variation by socioeconomic groups, with no particular trend evident between the two elements and social status.

It is possible that the developmental conditions implied by these indicators are specific to the adult survivors and that the experience of those who died in childhood was very different. Insight into which groups might have experienced greater mortality risks prior to adulthood may help to address this bias by identifying those most likely impacted by differential selective mortality.

5.3 The mortality of subadults

5.3.1 Parish burial data for subadults

How the risk of mortality across sub adulthood might vary by sex and socioeconomic status is assessed here using data from St. Bride's parish burial records.

These records pertain to individuals interred in the parish's upper burial ground and church (n=3596) as well as the lower burial group in Farringdon Street (n =5512). These two burial grounds are not only spatially separate, but present a clear socioeconomic divide as well. The upper burial ground and church was used by higher status individuals, and includes the crypt burials from which the St. Brides skeletal sample originates. The lower ground was used exclusively by the poorer members of the parish and is where the Farringdon skeletal sample were buried. Understanding how selective mortality might have exerted differential impacts on socioeconomic groups as well as males and females may help explain the frequencies of childhood stress indicators in the adult skeletal remains.

Kaplan-Meier survival analysis is conducted to assess whether survival curves differed between males and females under twenty years of age. Cumulative survival curves (Figure 5.1) do not differ significantly between males and females over subadult years: Log Rank (Mantel-Cox) $X^2 = 0.372$, df = 1, p = 0.542. In the first six months males have slightly decreased survival compared to females (the male vertical drop is longer), but in the next six months, at one year of age, females also experience relatively decreased survival, evidenced as the distance between the curves being minimised due to the female vertical drop being greater than males at this age. A similar pattern is maintained over sub adulthood.

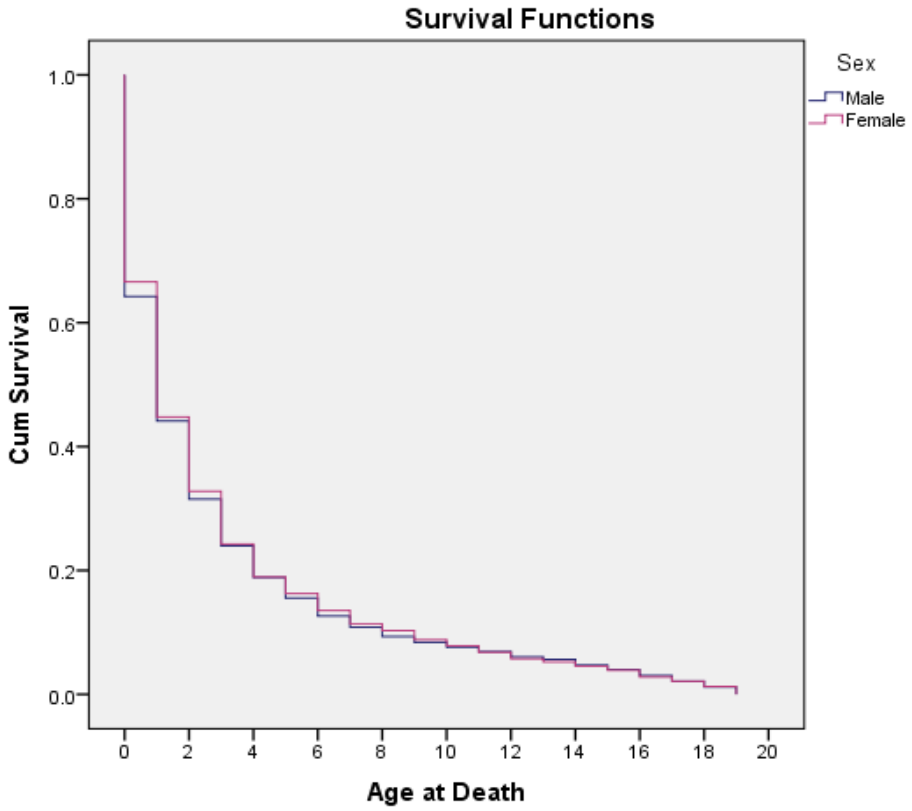

Figure 5.1 Kaplan-Meier survival curves for male and females under twenty years of age. Male n=1929, female n=1738.

While enamel hypoplasia and bone length in adult survivors showed no particular variation by socioeconomic status, the severity of cribrotic lesions may partially reflect social status. But this relationship only extended to the high status St. Bride's having the lowest crude prevalence of cribra orbitalia, while middle status St. Benet's displayed the highest. However, mortality risks suggest survival to adulthood may have been biased by socioeconomic status. Of individuals who died before twenty years, significantly decreased survival is evident for low status Farringdon children compared to children from higher status families buried in the church and upper burial ground; Log Rank (Mantel-Cox) $X^2 = 12.597$, df = 1, $p < 0.001$ (Figure 5.2). When mean survival times are compared, the average age at death for Farrington (2.62 years, 95% CI: 2.46-2.77) is lower than that for St. Brides (3.25 years, CI: 2.96-3.52),

suggesting a significant mean difference of seven to eight months. However, the Kaplan-Meier curves shown in Figure 5.2 suggest this difference was not apparent until two years of age, and most acute at four years, after which the curves are relatively parallel until seven years. Following this, differences in survival risks between the two groups diminish gradually until the curves converge at seventeen years.

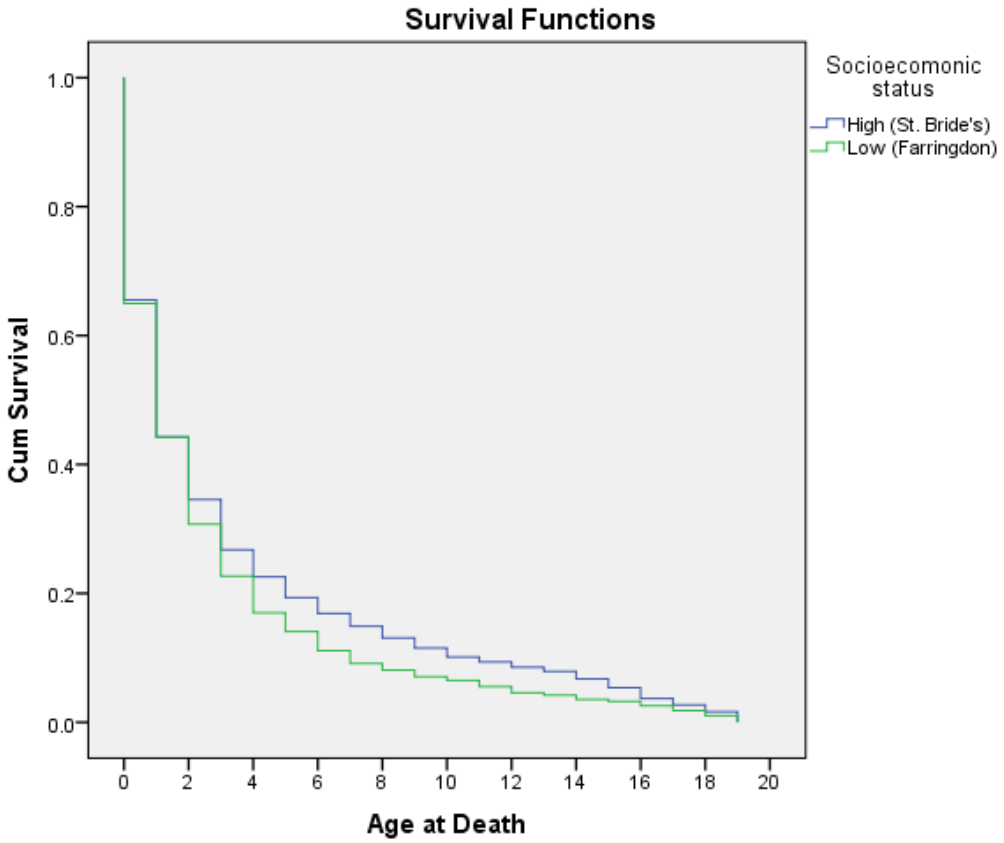

Figure 5.2 Kaplan-Meier survival curves for Farringdon and St. Bride's individuals who died prior to twenty years of age. St. Bride's n = 1215, Farringdon n= 2470

5.4 Interpreting variation in childhood environments

Results suggest that slight variation may have existed between the environments that male and females survivors experienced during childhood in terms of hypoplastic defects, while, conversely, frequencies of cribra orbitalia suggest they were likely similar. In contrast, frequencies of cribra orbitalia point to differences amongst the

socioeconomic groups, while hypoplastic defects suggest little differences existed. Further, mortality curves, based on burial records, indicate that socioeconomic status may have been a major influence - not only shaping the childhood environments of individuals in these samples, but also who was likely to survive to adulthood. This means that selective mortality may have influenced the frequencies of stress indicators reported in the adult survivors, particular affecting lower status individuals. Research investigating the health consequences of Spanish colonisation for an indigenous Mochica population in Peru found a lower risk of hypoplastic defects in adult survivors following colonisation (Klaus and Tam 2009). This was in contrast to heightened risks associated with other biological stress indicators, including porotic hyperostosis, growth velocity, bilateral periosteal new bone, and fertility (Klaus and Tam 2009). The authors suggest that the introduction of novel diseases, such as smallpox and measles, in conjunction with elevated biological stress initiated by colonisation, likely resulted in fewer children surviving these health insults. Consequently, the lower post-colonial risk of hypoplastic defects may actually reflect decreased childhood survivorship. Furthermore, enamel hypoplasia and cribra orbitalia may describe different types of stressors operating at various times within infancy and childhood, further complicating interpretations regarding childhood environments.

The environments suggested by skeletal and dental indicators in this research are probably not unusual for London during the 18th and 19th century. Cribra orbitalia was reported in 34% of adults in the Spitalfields crypt collection, who represent a middle status London sample of the same time period (Molleson and Cox 1993). Their prevalence lies within the range of frequencies for cribra orbitalia reported in this research, 13% to 49%. Hypoplastic defects are ubiquitous in these samples, occurring in 90% of individuals who survived to adulthood, however, this may also be typical for

this particular context. Work by King et al. (2005) reported all adults in their Spitalfields sample exhibited hypoplastic defects, although they scored the whole dentition, which likely explains the slightly higher prevalence. In addition, the Spitalfields individuals also had, on average, approximately two defects formed between two and six years of age (King et al. 2005). It would seem reasonable to assume that the frequencies of stress indicators reported in this study are typical for the time and place.

5.4.1 Variation by sex: infancy and childhood stressors

For those who survived to adulthood the frequencies of cribra orbitalia appear similar between males and females. Similar prevalence's between the sexes is not usual, particularly for lesions that are not active. In a survey of studies reporting frequencies of cribra orbitalia and porotic hyperostosis by sex, 24 out of 28 reviewed detected no difference between the sexes, while three reported higher frequencies in females (Stuart-Macadam 1998:49). Furthermore, as cumulative survival did not significantly differ between boys and girls it is unlikely that selective mortality biased frequencies reported in the adult survivors. In all likelihood, it is possible that the occurrences of cribrotic lesions noted in this research may reflect males and females simply experienced similar levels of exposures to causal stressors. Cribrotic lesions are generally considered indicative of micronutrient deficiencies (Stuart-Macadam 1985, 1987; Oxenham and Cavill 2010; Zariſa et al., 2016) and within this population it is likely that the majority of lesions formed before five years of age (Stuart-Macadam 1985; Lewis 1999). Lewis's (1999) work on the Spitalfields children reported most lesions occurred between six months and two years, coinciding with ages when historical sources suggest the weaning process was commonly implemented. These

results for cribra orbitalia suggest that in industrialised London, young boys and girls were likely exposed to similar levels of early causal stressors. Furthermore, if the lesions do reflect weaning practices, then it would suggest that boys and girls were treated the same in this regard.

Conversely, work on some of the same material as this research (Chelsea and Farringdon collections) argues that females, particularly of low status, were treated poorly compared to males, such as differential weaning practices favouring boys (Hughes-Morey 2016). Results in this research failed to detect any meaningful differences in standardised femoral and tibial lengths that would point to preferential treatment of boys. The difference between findings is probably because the assessment of growth stunting from final long bone lengths is problematic. However, in this analysis, males did display slightly more hypoplastic defects, on average, than females, suggesting some variation in their experience of stressors is evident.

5.4.2 The male biological disadvantage as a source of variation

This difference in hypoplastic defects could suggest either the male environment, or alternatively their response to threats within it, may have varied to that of females after approximately two years of age. In other bioarchaeological studies that report higher frequencies of defects in males, various explanations are offered for the difference (Van Gerven et al., 1990; Zhou and Corruccini 1998; Saunders and Keenleyside 1999; Palubeckaite et al., 2002; Berbesque and Doran 2008, Gamble 2017). Some suggest that females likely experienced fewer childhood stressors (Van Gerven et al.1990), while others suggest that due to preferential treatment of boys more males survived with defects (Zhou and Corruccini 1998; Palubeckaite et al. 2002). A

study of mediaeval Danish and Lithuania groups only found significant sex differences in the high status aristocratic group, where more males had defects than females (Palubeckaitė et al. 2002). The authors suggest that males may have been treated preferentially only in the high status medieval group, allowing more males with defects to survive to adulthood, while the lower status rural and urban groups did not favour one sex in particular (Palubeckaitė et al. 2002:198). Another possibility is that medieval weaning practices varied amongst the groups where higher status children were more likely to receive supplementary foods at an earlier age (Stevens et al. 2009), which due to an increased risk of infection could disproportionately disadvantage males. In stressful environments, increased frequencies of hypoplastic defects in males are suggested to be predicable, assuming boys are not afforded preferential treatment compared to girls (Guatelli-Steinberg and Lukacs 1999:82). Few researchers, however, directly point to the likelihood of increased biological susceptibility of boys to explain higher frequencies of hypoplastic defects and tend to consider male preferential treatment as a more likely explanation, although it is sometimes tentatively suggested as a possibility (Saunders and Keenleyside 1999; Berbesque and Doran 2008).

The biological male disadvantage is well documented, beginning in utero males are at greater risk of premature birth and respiratory conditions, but also at greater risk of infectious diseases during infancy and childhood (Zeitlin et al. 2002; Bouman et al. 2005; Drevenstedt et al. 2008). While it is also possible that gender differences regarding risk of exposure to stressors might have been operating on children between two and six years, this does not discount the likelihood that a male biological disadvantage to infection may explain the greater number of hypoplastic defects in males. Due to the high risk of infectious disease exposure in London during the Industrial Revolution, all individuals likely experienced high risks of exposure to

pathogens (Landers 1993) and it is not unexpected that male children may have been slightly more biologically vulnerable than females to stressors and the formation of hypoplastic defects. These results could imply that early stressors associated with cribra orbitalia, such as poor quality weaning foods, were similar for boys and girls, but boys may have been more likely to experience stressors causal to enamel hypoplasia. Considering boys can be more vulnerable to infections than girls (Zeitlin et al. 2002; Bouman et al. 2005; Drevenstedt et al. 2008), an aetiology of infectious disease for many of the hypoplastic defects reported in these samples would seem likely, as has been suggested by other researchers (Goodman et al. 1991:780; Brook and Smith 1998:154)

5.4.3 Variation amongst socioeconomic groups

Socioeconomic status does not appear to influence occurrences of hypoplastic defects or variation in femoral and tibial lengths, but variation in cribra orbitalia and porotic hyperostosis was evident. However, these frequencies in adult survivors may have been biased by selective mortality. The number of individuals with cribrotic lesions was lowest in higher status St. Bride's, while individuals form middle status St. Benet's had the highest crude prevalence. Middle to high status Chelsea and low status Farringdon were intermediate for these lesions, which for all samples ranged from 13% to 49% of individuals affected. Other work that detected higher frequencies of cribrotic lesions amongst lower socioeconomic status groups suggested that iron and vitamin B_{12} deficiency due to variation in parasite loads, as well as anaemia of chronic disease, was likely responsible (Sullivan 2005). No cribrotic lesions were active in the London

samples, suggesting these lesions may be associated with infant and childhood conditions, as suggested by Stuart-Macadam (1985) and Lewis (1999).

5.4.4 Cribra orbitalia and weaning practices

Other researchers analysing the Spitalfields sample also speculate that a deficiency in dietary iron might be causal to cribra orbitalia, particularly if low maternal iron levels are involved during lactation as well as truncated weaning and inadequate supplementary foods. Molleson and Cox (1993). Lewis's (1999) work suggests that weaning was complete by two years for children in industrialised London. More recent stable isotope analysis of Spitalfields individuals supports this timing, but also suggests some infants may have been transitioned to artificial feeding, in lieu of breast milk, from birth (Nitsch et al. 2011). During this period, colostrum was also commonly withheld in the belief that it was unhealthy, denying the infant of important antibodies and immunoglobulins (Fildes 1986). Professional wet nurses were often paid to feed infants, but unless the family could afford to employ a dedicated nurse, the infants may have been one of many competing for nourishment (Fildes 1986; Stevens et al. 2009). In addition, the fashion was to completely wean infants early, often by six months in favour of pap or panada, poor quality nutritional substitutes usually consisting of bread soaked in cow's milk, broth, or beer (Fildes 1986; Hervada and Newman 1992; Obladen 2014). It is possible that the quality of replacement and supplementary foods associated with weaning may have reflected a social gradient, with poorer parents less able to provide foods that were adequately nutritious.

The lower frequencies of cribrotic lesions in higher status St. Brides may result from more of these families employing dedicated wet nurses as well as possibly using

higher quality weaning foods (Fildes 1986; Stevens et al. 2009). St. Benet's individuals, who had the highest frequencies of cribrotic lesions as well as the only incidences of porotic hyperostosis, stand out from the other samples. It is possible that these individuals experienced a more adverse early environment, possibly reflecting weaning practices and risks of exposures, either nutritional or parasitism, but which differed somewhat to the other London samples. Lower status Farringdon had frequencies similar to middle to high status Chelsea. However, the frequencies of cribrotic lesions in the lower status groups may have been influenced by selective mortality. According to burial records, lower status children experienced decreased survival compared to higher status subadults. Therefore, if the stressors causal to cribra orbitalia also influenced subadult mortality, which research suggests is the case (for example, Mittler and van Gerven 1994; Lewis 2002) these frequencies are likely to be underestimated in the Farringdon adults. Subadult mortality risks cannot be obtained for Chelsea and St. Benet's. This is unfortunate, particularly as the exceptionally high frequencies of cribra orbitalia and occurrences of porotic hyperostosis in the St. Benet's groups suggest they may have experienced developmental conditions where micro nutrients deficiencies, such as iron or vitamin B12, were particularly prevalent. Yet, St. Benet's did not differ significantly to the other groups in either hypoplastic defects or bone length. So even if frequencies of cribra orbitalia have been impacted by selective mortality causing its prevalence in the lower status Farringdon adults to be underestimated, St. Benet's still stands out as exceptional.

5.4.5 Apparent similarities and selective mortality

The frequencies of hypoplastic defects in adults were similar between the socioeconomic groups, suggesting few individuals escaped childhood health insults

regardless of social status. Other studies that have directly compared frequencies of hypoplastic defects amongst groups of differing socioeconomic status have comparable results. Using historical Portuguese data, Amoroso et al. (2014) found similar frequencies of defects, as well as mean numbers per individuals, in high and low socioeconomic groups. Work by Palubeckaitė et al. (2002) detected no difference in either frequencies or mean defect numbers between a high status aristocratic sample and a lower status rural sample. In a lower status urban group, however, frequencies and mean numbers of defects were higher than in either of the other two groups (Palubeckaitė et al. 2002).

In addition to enamel hypoplasia, femoral and tibial lengths also did not differ significantly by socioeconomic status in this research. Measurements were also very similar to femur and tibial lengths from the Spitalfields study, whose assessments were within the ranges reported in this study (Molleson and Cox 1993). It is possible that assessments of both hypoplastic defects and bone lengths in the adult survivors was biased by selective mortality. It is also conceivable that similarities in femoral and tibial lengths between the socioeconomic groups could reflect issues with using final bone lengths as an indicator of developmental environments (see Ribot and Roberts 1996; Mays 1999; Prentice et al. 2013). However, the relationship between enamel hypoplasia and heightened subadult mortality risks is more certain (Cook and Buikstra 1979; Stodder 1997; Cucina, et al. 2000; Slaus 2000; Klaus and Tam 2009; Mendez Colli et al. 2009).

The question that then arises is if adult frequencies of both cribra orbitalia and enamel hypoplasia were impacted by selective morality, why does enamel hypoplasia show less variation amongst the social groups than cribra orbitalia? One explanation is that the stressors these indicators reflect might have dissimilar aetiologies that were

differentially impacted by socioeconomic status. For example, if cribra orbitalia does reflect micronutrient deficiencies associated with weaning practices and quality of supplementary foods, then social status and differential access to adequate food stuffs would be expected to be particularly influential. Conversely, if hypoplastic defects are more indicative of infections, between two and six years of age, and all children were likely at risk of exposure, then it might be expected to display less of a social gradient.

5.5 Childhood health experiences in industrialised London

During the Industrial revolution, growing disparities between socioeconomic classes in London may have profoundly influenced childhood health risks and outcomes. Burial records suggest that low status children faced a greater mortality risk than higher status children, but little variation was evident between girls and boys. Furthermore, cribra orbitalia may indicate socioeconomic variation in weaning food quality and practices that particularly disadvantaged poorer children. While high frequencies of hypoplastic defects, formed between two and six years of age, may reflect that all children were at risk of infection in this disease prone environment. Although it is likely that lower status children were more vulnerable to infection than higher status children, it appears that sex also had a marked influence. In this infectious environment boys may have been more slightly more susceptible to physiological insults, although not necessarily death, than girls.

Having investigated how the developmental environments and risks of adverse childhood health may have varied by sex and between the socioeconomic groups, the adult environments needs to be explored next. Once these relationships and likely influences shaping adult outcomes have been elucidated at the group level, factors

relevant at the individual level can be better assessed. Considering how risks may appear to alter between early and later life can suggest mechanisms, such as acquired immunity and scarring, which may be operating over the life course. Knowledge of the childhood and adult environments at the group level provides context in which to understand the individuals.

CHAPTER SIX: ADULT ENVIROMENT RESULTS

6.1 Introduction

In this chapter, skeletal lesions associated with adverse health experienced in adulthood are investigated. I attempt to gain insight into how the broader adult environments may have varied between males and females as well as the different socioeconomic groups: high status St. Brides, middle to high status Chelsea, middle status St. Benet's, and low status Farringdon. Frequencies of periosteal new bone formation are investigated to determine if belonging to a particular group might increase the likelihood of having lesions, including whether active, mixed, or healed lesions are most likely to occur. Periodontitis is assessed, including the severity of the condition, and how this might vary by group. How mortality risks may have varied are investigated using parish burial data for adults over nineteen years, including their possible influence on frequencies of adult stress indicators. Analysis of three specific causes of death common to this period, tuberculosis, chorea, and smallpox is undertaken, including how the risks they posed may have varied by sex and socioeconomic status.

Age at death from the skeletal samples is not used to assess group differences in mortality risks as, due to selection bias, the samples may not accurately reflect real differences in the risk of death between the groups. Skeletal age at death estimates, however, are meaningful when individual associations between early and later life health outcomes are sought. Building upon information of the development environment in the preceding section, these data should suggest how health risks and outcomes may have varied between groups across the life course. Collectively, they should help develop a picture of the various environments that the living may have

experienced, providing context for interpreting possible links between early and later health outcomes at the individual level.

6.2 Periosteal new bone formation

While variable occurrences of periosteal new bone may reflect differential group risks of trauma or infection to the periosteum, whether the lesions are in an active, mixed, or healed state at death may indicate heterogeneous levels of frailty between groups. In these skeletal samples, males and females were very similar in both the likelihood of periosteal new bone lesions in general, as well as their particular state of healing (Table 6.1). Approximately two thirds of both males and females did not have any new bone formations. Amongst those with lesions, most had healed or represented mixed lesions. A chi square goodness of fit test confirmed that frequencies of lesion categories did not vary significantly from those expected in a random distribution (X^2 = 0.615, df = 3, p = 0.897). This was also the case when only individuals with lesions were tested (X^2 = 0.480, df = 2, p = 0.787).

Table 6.1 Comparison of various states of periosteal new bone formation, including absence, by sex

		Periosteal new bone lesions			
		None	Active	Mixed	Healed
Male	% within Sex	64.1%	6.8%	14.6%	14.6%
	Count	66	7	15	15
	Std. Residual	0.2	0.0	0.2	-0.5
Female	% within Sex	61.5%	6.6%	13.2%	18.7%
	Count	56	6	12	17
	Std. Residual	-0.2	0.0	-0.2	0.5

A similar pattern of periosteal lesions is evident among the cemetery groups (Table 6.2). Although the standardised residuals suggest that Chelsea may have a higher than expected percentage of individuals with active lesions, overall this was not sufficient to reach statistical significance (Fisher-Freeman-Halton exact p=0.057). When only individuals with lesions were considered, the differences were still not significant (Fisher-Freeman-Halton exact p=0.164). So overall the frequencies of periosteal new bone lesions are consistent with random differences among the samples, suggesting no group was significantly more likely than another to have lesions of any type.

Table 6.2 Comparison of various states of periosteal new bone formation, including absence, by cemetery group.

		Periosteal new bone lesions			
		None	Active	Mixed	Healed
St. Bride's	% within Cemetery	61.0%	2.4%	9.8%	26.8%
	Count	25	1	4	11
	Std. Residual	-0.2	-1.0	-0.7	1.6
Chelsea	% within Cemetery	59.3%	13.6%	15.3%	11.9%
	Count	35	8	9	7
	Std. Residual	-0.4	2.1	0.3	-0.9
St. Benet's	% within Cemetery	53.3%	4.4%	22.2%	20.0%
	Count	24	2	10	9
	Std. Residual	-0.8	-0.6	1.5	0.6
Farringdon	% within Cemetery	78.0%	4.0%	8.0%	10.0%
	Count	39	2	4	5
	Std. Residual	1.3	-0.7	-1.1	-1.1

6.3 Periodontitis

Although periosteal lesions do not appear to markedly affect any group in particular, periodontitis may offer another way to investigate levels of frailty between groups. Periodontitis, particularly severe occurrences in the form of periodontal pockets, have been associated with chronic morbidities as well as immunologically compromised individuals (Scannapieco et al. 2003; Crespo et al. 2016). As periodontitis is scored for each septa, variation in severity scores are anticipated within individuals. In addition, only severity states representing at least 25% of an individual's observable septa are analysed, allowing the more predominant states present within an individual to be focused upon. This means, for example, an individual may have 80% of observable septa displaying periodontitis and 20% that are 'healthy', or without periodontitis,

which is under the 25% threshold to report. For convenience, the term ‘healthy’ refers to septa that do not display bone loss indicative of periodontitis, but which may include milder gingivitis.

On average, the number of observable septa per individual ranged from approximately 15 to 17, with the higher status cemetery groups of St. Bride’s and Chelsea showing slighter fewer intact septa than St. Benet’s and Farringdon (Table 6.3). Most people exhibited periodontitis to some degree with 77% of individuals having at least 25% of their observable septa showing periodontitis, while 17% exhibited periodontal pockets. Of the individuals with a least five observable septa (n=169) only four individuals (2%) were completely free of periodontitis, with only gingivitis or healthy septa.

Table 6.3 Counts of individuals with at least 5 observable septa including mean and median number of observable septa per group and percentages of individuals with over 25% of observable septa displaying no periodontitis (healthy), periodontitis, and pocket lesions.

		Male	Female	St. Bride’s	Chelsea	St. Benet’s	Farringdon	Total
Individuals	n	90	78	36	41	45	47	169
Observable Septa	Mean	16.08	16.95	15.50	15.29	17.53	17.26	16.48
	SD	7.00	7.37	6.93	7.03	7.83	6.70	7.15
	Median	15.50	16.50	14	16	17	16	16
Healthy		52.2%	66.7%	51.2%	66.0%	63.9%	55.6	59.2%
Periodontitis		80.0%	74.4%	85.4%	68.1%	77.8%	80.0	77.5%
Pockets		24.4%	9.0%	7.3%	19.1%	11.1%	28.9	17.2%

Chronic periodontitis tends to accumulate with age, as is evident in Figure 6.1 (left), where a corresponding decrease in the number of individuals with at least 25% of septa lacking periodontitis, or healthy, is evident. Pocket lesions represent a more severe form of periodontitis and do not track with age in the same way (Figure 6.1, right), possibly reflecting their association with adverse health conditions. Therefore, to minimise associations that reflect normal age related increases in chronic periodontitis lesions, analysis will focus only on the distribution of pocket lesions amongst the groups.

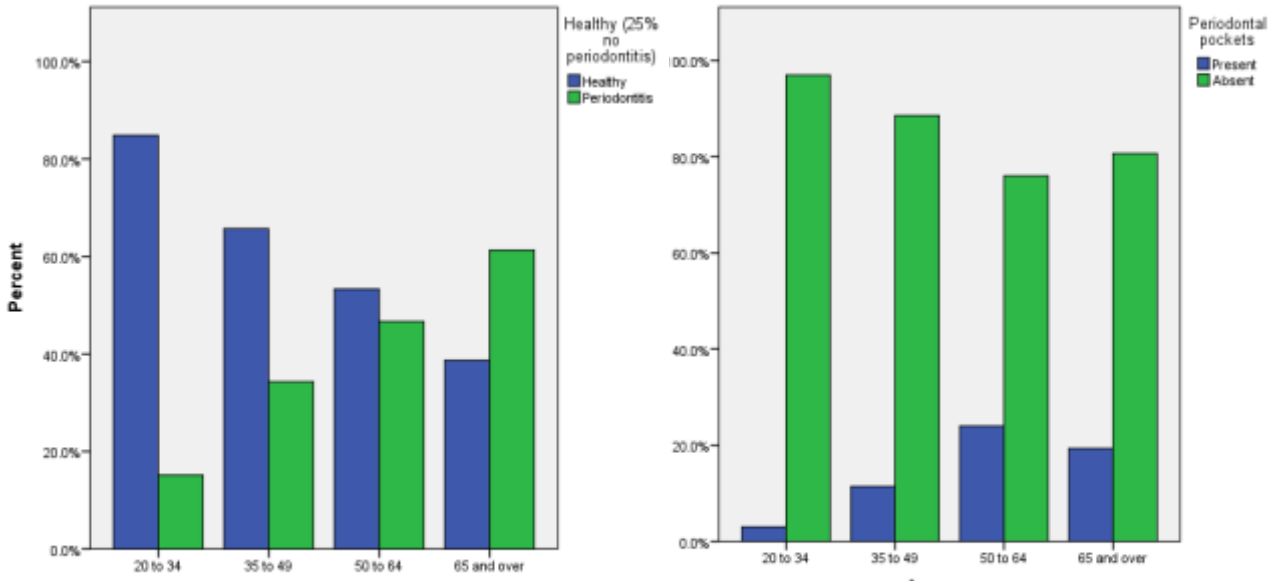

Figure 6.1 Left, frequencies of individual's with healthy (no periodontitis) and periodontal lesion affecting at least 25% of septa. At right, presence or absence of individual with pocket lesions affecting at least 25% of septa.

Females had significantly fewer pocket lesions than males ($X^2 = 7.199$, df = 1, p = 0.007), as evidenced by the standardised residuals (Table 6.4). Frequencies also differed significantly by cemetery group ($X^2 = 8.369$, df = 3, p = 0.039). Individuals from St. Brides were less likely than expected to have periodontal pockets, while higher than expected frequencies were found in the Farringdon sample.

Table 6.4 Frequencies of individuals present and absent for at least 25% of observable septa with periodontal pockets by sex and cemetery groups.

		Sex		Cemetery			
		Male	Female	St. Bride's	Chelsea	St. Benet's	Farringdon
Present	% within pockets	75.9%	24.1%	10.3%	31.0%	13.8%	44.8%
	Count	22	7	3	9	4	13
	Std. Residual	1.7	-1.8	-1.5	0.2	-.9	2.0
Absent	% within pockets	48.6%	51.4%	26.2%	29.0%	22.8%	22.1%
	Count	70	74	38	42	33	32
	Std. Residual	-0.8	0.8	0.7	-0.1	0.4	-0.9

6.4 Adult markers of health – an assessment

While no significant variation between sexes or among cemetery groups was found for periosteal new bone lesions, among individuals with periodontal pockets, reflective of more severe periodontitis, marked differences were seen across groups. Males were more likely than females to have pocket lesions affecting at least 25% of observable septa, while high status St. Bride's had fewer than expected in contrast to low status Farringdon who had the highest frequencies suggesting that periodontitis particularly the pockets could be assumed to reflect socioeconomic factors. However, how these frequencies might be influenced by adult mortality risks still needs to be considered before their value as frailty indicators can be ascertained.

6.5 Parish burial data

6.5.1 Survival analysis

Burial records from St. Bride's parish include adult individuals (twenty years and over) interred in the higher and lower status burial grounds and from which the St.

Bride's and Farringdon skeletal samples are derived, respectively. As reported in Figure 6.2, Kaplan-Meier survival analysis show males (n = 2670) experienced significantly decreased cumulative survival across adulthood compared to females (n = 2791) (Log Rank Mantel-Cox X^2 =65.940, df = 1, $p < 0.001$). The male median survival time was 50 (SE = 0.42) years, compared to 54 (SE = 0.60) years for females. Some age rounding is apparent for both sexes at 40, 50, 60, and 70 years, but this doesn't impact the overall trend. Until 35 years the increased female survival is very slight, but the curves diverge increasingly until 50 years. The greatest difference in mortality risks is from 50 to 70 years, after which they begin to converge. Although differential selective mortality likely operated across adulthood, it is expected to have been most acute between 50 and 70 years of age, which accords with the skeletal age group of 50 to 65 years.

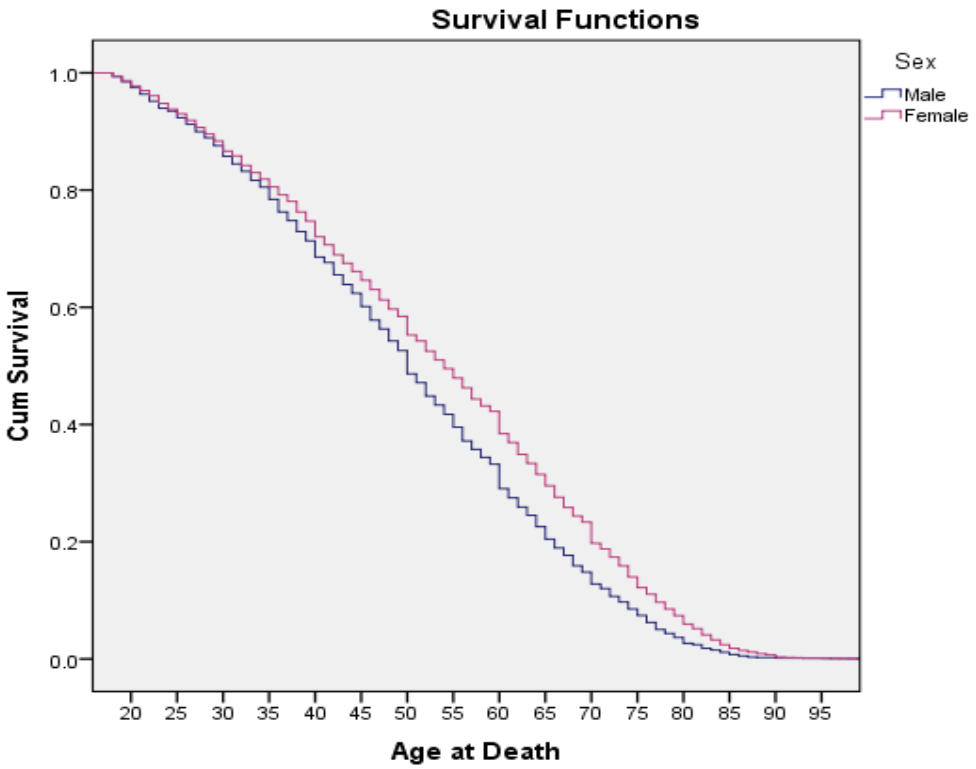

Figure 6.2 Kaplan-Meier survival curves for adult male and females based on St. Bride's parish burials records.

Although cumulative survival varied significantly by sex, there was no statistically significant difference by socioeconomic status in the parish. Kaplan-Meier survival curves (Figure 6.3) do not significantly differ between the higher and lower status groups (Log Rank Mantel-Cox $X^2 = 2.452$, df = 1, p = 0.117). The risk of death in adulthood was not particularly influenced by socioeconomic status in this parish, despite a clear economic divide and a difference in childhood survivorship by socioeconomic status.

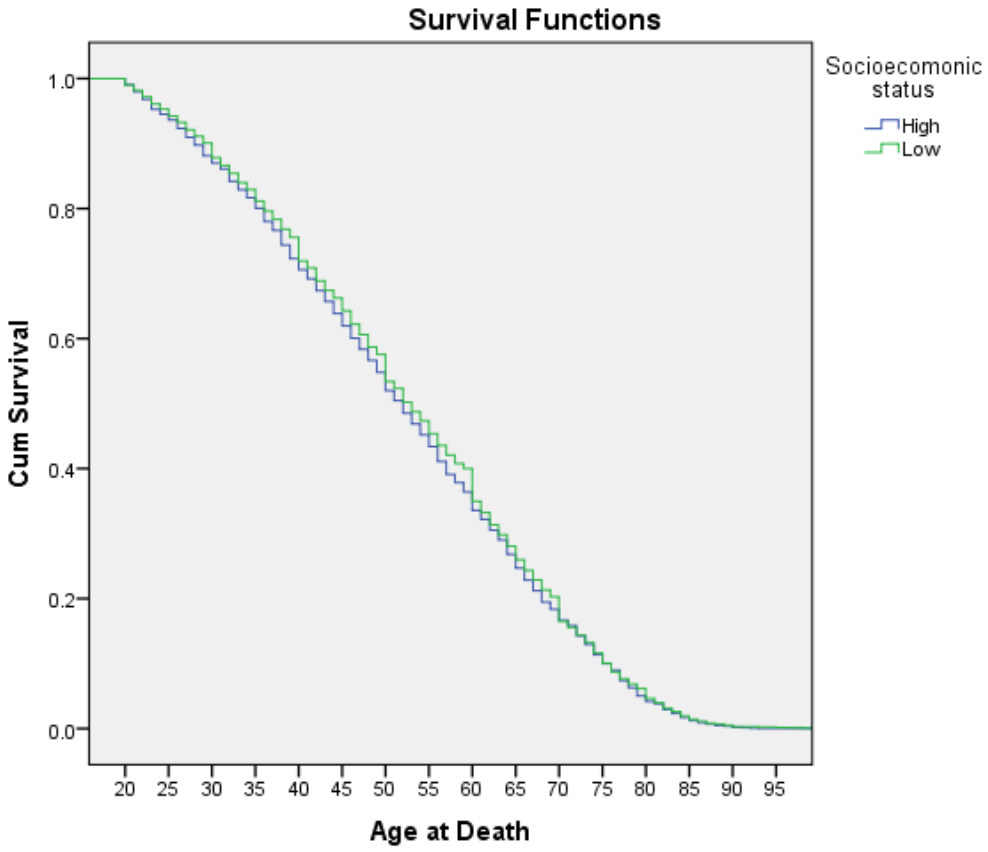

Figure 6.3 Kaplan-Meier survival curves for high and low socioeconomic adults based on St. Bride's parish burials records

6.5.2 Three specific causes of death

Causes of death that might be, at least, partly responsible for this differential survival risk may be relevant to understanding connections between early and later life health outcomes. Here adult deaths reported as either tuberculosis (*Mycobacterium*

tuberculosis), cholera (*Vibrio cholera*), or smallpox (*Variola major virus*) have been isolated for analysis. Amongst these three diseases (n=626), 87% of deaths were attributed to tuberculosis, 8% to cholera and 5 % to smallpox. It is important to note that the risks of death being compared are specific only to these causes, and so excludes the many other causes of death that people within the parish succumbed to. Also, because the number of individuals at risk is unknown, mortality rates cannot be calculated. However, it is possible to know how the risk of death varied between cholera, tuberculosis, and smallpox burials within the parish and if this risk varied by sex or socioeconomic groups. As the risk of death from certain causes can vary by age across adulthood, disease frequencies are also analysed by age group.

The frequencies of burials due to tuberculosis, cholera, and smallpox in each age group for males and females are reported in Table 6.5. Clearly tuberculosis was responsible for the greatest proportion of these deaths, with the worst toll exerted on the youngest adults and then gradually declining with age. Cholera shows a reverse trend, the heaviest toll is amongst the oldest individuals. Smallpox killed the most during early adulthood and then declines rapidly compared to the other infections. The frequencies of these infections are significantly associated with sex ($X2 = 10.074$, $df = 2$, $p = 0.006$). Judging from information in Table 6.5, both cholera and smallpox appear to have disproportionately affected females. Cholera shows the greatest consistency in the sex associated differential across age groups and has the largest residuals for total deaths. When analysed by age, only the youngest adult group suggests significant variation (Fisher-Freeman-Halton exact, $p = 0.035$), with the sex differential mainly driven by smallpox followed by cholera. Tuberculosis did not appear to discriminate as much, killing males and females with nearly equal ferocity. Although not statistically

significant, more males were at slightly risk of dying from tuberculosis in all age groups than females judging from the standardised residuals.

Table 6.5 Frequencies of burials due to tuberculosis, cholera, and smallpox by sex and age groups.

	Age groups									
	20 - 34		35 - 49		50 - 64		65+		Total	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Tuberculosis										
% w/n	93.9	83.3	90.9	88.0	88.4	82.3	76.9	52.4	91.0	82.3
Count	123	90	100	81	61	51	10	11	294	233
Std. Resid.	0.6	-0.6	0.1	-0.2	0.3	-0.3	0.7	-0.5	0.8	-0.8
Cholera										
% w/n	2.3	5.6	5.5	9.8	8.7	12.9	23.1	42.9	5.6	11.3
Count	3	6	6	9	6	8	3	9	18	32
Std. Resid.	-0.9	1.0	-0.8	0.8	-0.5	0.5	-0.7	0.6	-1.7	1.8
Smallpox										
% w/n	3.8	11.1	3.6	2.2	2.9	4.8	0.0	4.8	3.4	6.4
Count	5	12	4	2	2	3	0	1	11	18
Std. Resid.	-1.4	1.6	0.4	-0.4	-0.4	0.4	-0.6	0.5	-1.1	1.2

Although cumulative survival over adulthood did not differ by socioeconomic status the risk of death posed by cholera, tuberculosis, and smallpox certainly did. Frequencies of individuals from the higher and lower status burial grounds along with the standardised residuals for each disease are displayed in Table 6.6. Similar age related trends by sex are evident in the two different cemetery groups, but the impact of the different disease types differed significantly between the low and high status groups. Overall, both cholera and smallpox disproportionately affected the lower status

group; $X^2 = 14.633$, df = 2, p = 0.001. The higher risk of smallpox for younger adults already noted above, is seen here as a phenomenon within the low status group. Risks are significantly higher for this group in both the 20-34 year olds (Fisher-Freeman-Halton exact, p=0.030) and the 35 to 49 year olds (Fisher-Freeman-Halton exact, p=0.013). The standardised residuals show that cholera followed a similar, but weaker trend.

Table 6.6 Frequencies of burials due to tuberculosis, cholera, and smallpox by socioeconomic status (SES) and age groups.

	Age groups									
	20 – 34		35 – 49		50 – 64		65+		Total	
	SES		SES		SES		SES		SES	
	High	Low	High	Low	High	Low	High	Low	High	Low
Tuberculosis										
% w/n Sex	93.9	85.0	96.6	84.7	84.0	86.4	85.7	45.0	92.5	82.9
Count	108	108	84	100	42	70	12	9	246	287
Std. Resid.	0.5	-0.5	0.7	-0.6	-0.1	0.1	1.1	-1.0	0.9	-0.8
Cholera										
% w/n Sex	3.5	3.9	3.4	10.2	14.0	8.6	14.3	50.0	6.0	9.8
Count	4	5	3	12	7	7	2	10	16	34
Std. Resid.	-0.1	0.1	-1.3	1.1	0.7	-0.6	-1.3	1.1	-1.2	1.1
Smallpox										
% w/n Sex	2.6	11.0	0.0	5.1	2.0	4.9	0.0	5.0	1.5	7.2
Count	3	14	0	6	1	4	0	1	4	25
Std. Resid.	-1.8	1.7	-1.6	1.4	-0.7	0.5	-0.6	0.5	-2.4	2.1

Analysis of the three specific causes of death demonstrates that certain infections may disproportionately impact males and females in some circumstances, while in other stipulations, lower socioeconomic individuals. Tuberculosis was

responsible for most deaths, but less discriminate and heavily impacted all ages. Cholera maintained a consistent bias towards females and lower socioeconomic status individuals. Smallpox was responsible for fewer deaths overall, but most impacted females under 35 years of age and lower socioeconomic individuals under 50 years.

6.6 Measures of adverse health in adult males and females

Periosteal new bone formation is discussed generally in terms of sex and socioeconomic status, as this did not vary between groups. Other measures of adverse adult health, including periodontitis, mortality risks, and infectious disease are discussed first in terms of male and female differences and then how outcomes are influenced by socioeconomic status.

6.*6.1 Periosteal new bone formation*

In these skeletal samples, 37% of all individuals showed signs of periosteal new bone formation, with approximately 82% of lesions either healed or in the process of healing at the time of death. Compared to frequencies reported in a medieval urban sample in York, where 31% of adult individuals had periosteal new bone formations, the Londoners show a slightly higher crude prevalence (Grauer 1993:206). However, the York individuals showed a slightly higher prevalence of active lesions, 23% (Grauer 1993: 206), compared to 18% in the London sample. Both these samples display higher frequencies than were reported in a medieval rural group, Wharram Percy, where only 8% of individuals had periosteal new bone lesions (Mays 2010: 214). In contrast, 64% of lesions at Wharram Percy were active (Mays 2010: 215). Mays (2010) suggests that the difference in frequencies between the medieval urban and rural samples may reflect

the more infectious environment of the unsanitary town. Lower levels of exposure to pathogens could mean rural people were less immunologically equipped to resist infection, explaining why a higher prevalence died with active lesions (Mays 2010). In a study that scored the tibia for periosteal new bone lesions in medieval Londoners, 29% of adults had lesions, all of which showed signs of healing (DeWitte 2014:41). These studies, including this research, suggest that individuals living in urban environments may be more prone to periosteal new bone lesions, but also more likely to die with healed or partially healed lesions. Furthermore, individuals of industrialised London, analysed in this study, had slightly higher frequencies than reported in the medieval urban samples, possibly reflecting the increased infectious and unsanitary nature of the post medieval London environment.

Males and females do not appear to vary in their likelihood of periosteal new bone lesions, including the state of healing at the time of death. Furthermore, the distribution of periosteal lesions appears to be quite random amongst the socioeconomic group. Unlike subadult cumulative survival (determined from burial records), adult survival did differ significantly by sex, with males experiencing decreased survival compared to females. However, the periosteal lesions were also acquired during adulthood, so total frequencies are unlikely to have been influenced by selective mortality (although if analysed by adult age at death they might). This could suggest that main influence under riding periosteal new bone formation is the nature of the environment as a whole, rather than biosocial factors, such as sex, gender, or socioeconomic position.

6.*6.2 Periodontitis*

Unlike periosteal lesions, frequency of severe periodontitis differed between the sexes and amongst socioeconomic groups. Overall, 17% of individuals in the samples had severe periodontitis, but males were more than twice as likely to have the condition as females.

Modern clinical studies of periodontitis note adult males are more prone to severe periodontitis than females (Grossi et al. 1994; Grossi et al. 1995; Pihlstrom et al. 2005). Several reasons have been forwarded to explain the male excess in this disease, including an inherent male susceptibility and behavioural practices that may be more common in males than females (Grossi et al. 1994; Grossi et al. 1995). For example, the use of tobacco products, including smoking, chewing, and snuff, are high risk factors associated with periodontitis (Grossi et al. 1994; Pihlstrom et al. 2005). As increased occurrences of pocket lesions have been suggested to reflect a compromised immune system (Garcia et al. 2001; Pihlstrom et al. 2005; Igari et al. 2014; Crespo et al. 2016), the increased male risk accords, superficially at least, with their relatively higher adult mortality risk evident in the parish burial records.

6.*6.3 Infectious disease*

The increased survival of adult females noted from burial records, occurred despite certain causes of death appearing to favour them over males. Out of the three infectious diseases extracted for study, more females than males appear to have been at risk of cholera and smallpox especially during early adulthood. Tuberculosis did not appear selective. Although when pregnant, females may be slightly more susceptible to smallpox, generally they are not more biologically vulnerable to either smallpox or cholera than males (Fenner et al. 1988; World Health Organization 2007). This suggests

gender roles may have placed more females at greater risk either through increased exposure to the pathogens or through a greater proportion of adult females, such as rural immigrants, being immunologically naïve to the pathogens. As smallpox confers lifelong immunity to those previously infected (Fenner et al. 1988), adult fatalities are most likely to occur among those who were not previously exposed. This could point more to the role of immunological naivety as driving the higher adult female risk. Adult males may have been at greater risk of death in general, but females likely experienced greater risks from certain causes, such as smallpox and cholera.

6.7 **Socioeconomic status and adverse health measures**

6.*7.1 Periodontitis*

The likelihood of severe periodontitis varied significantly amongst the socioeconomic groups. Overall, Farringdon had more individuals with these severe lesions than expected, while St. Bride's had significantly fewer. Frequencies found at Chelsea and St. Benet's were intermediate to these two groups. It is possible that periodontitis is related to social behaviours, which varied by sex and class, such as smoking (Grossi et al. 1995; Nunn 2003; Pihlstrom et al. 2005). An analysis of dental pipe facets, which indicate an individual was a habitual pipe smoker and appear frequently in these skeletal samples, could help resolve this question. Alternatively, the frequencies of severe periodontitis could indicate that lower socioeconomic status individuals experienced higher risks of chronic or adverse health in adulthood than higher status individuals. While St. Bride's and Farringdon did not differ in their cumulative survival across adulthood (based on burial records), it is possible that adverse or chronic health conditions presented a greater threat to the poorer Farringdon individuals, reflected in their higher risk of severe periodontitis. Recent research, for

example, has suggested a two way link between periodontitis and tuberculosis (Sharma et al. 2016), a disease that was rampant in London during this period. Conversely, while the differential risks of severe periodontitis amongst the socioeconomic groups are seem in other infectious diseases in this research, tuberculosis was not one of them.

6.*7.2 Infectious disease*

Burial records do suggest, however, that lower status Farringdon individuals were at greater risk of mortality from cholera and smallpox. A disproportionately high number of smallpox deaths occurred in the lower status burial ground, with those less than 50 (particularly less than 35 years) most affected. Cholera also had considerable impact on the lower status group, though not as strongly as smallpox. The cholera bacterium (*Vibrio cholera*) is spread through contaminated water and food, and most frequently associated with overcrowded and unsanitary living conditions (Glass and Black 1992). Therefore, it is unsurprising that deaths due to cholera disproportionately impacted Farringdon. The disease does confer immunity for several years post infection such that subsequent exposures elicit a milder immune response with a lower risk of death (Levine and Pierce 1992).

Susceptibility to the smallpox virus (*Variola major*) is not particularly related to socioeconomic differences, such as poor nutrition, in contrast to cholera and tuberculosis (Landers 1993). Therefore, contracting the virus is mostly governed by the risk of exposure. The disease was endemic to London during his period and it is unlikely that any person who lived in the city for more than several years would have been able to avoid contact with the smallpox virus at some point, regardless of wealth (Landers 1993). So, although smallpox mortalities amongst the adults were not as high as other diseases, it is useful as a marker of migrants (Landers 1993; Davenport et al.

2011). One of the possibilities in this study is that immunological nativity may have an important role in the linkage between childhood and adult health.

The similarities in risks of tuberculosis between higher and lower socioeconomic classes is curious as the disease is reported to disproportionately impact lower status groups (Landers 1993: Barter et al. 2012; Oxlade and Murray 2012). Considering the impact of tuberculosis during this period, for example one quarter of Europeans are estimated to have died from tuberculosis in the first half of the 19th century (Smith 2003), a variation in risks by socioeconomic status should be detectable. The chronic nature of the disease's progression, however, may have influenced where people who died with the disease where finally buried. The pathogenesis of *Mycobacterium tuberculosis* means that the disease progresses relatively slowly, over months and often years, unlike smallpox or cholera (Smith 2003). It is possible that if a higher proportion of lower status groups were migrants then they may have been more likely to return to their home regions once they contracted the disease, particularly if they were unable to work (Landers 1993). This would have the effect of underestimating the number of people with tuberculosis when assessments are based on London burial records.

6.*7.3 Mortality risks*

Outward migration of individuals with tuberculosis could also explain the similarities in adult cumulative survival curves between higher and lower socioeconomic groups derived from parish records. The same pattern of mortality risks was reported in work by DeWitte et al. (2016) who used hazard analysis to assess mortality risks across the life course in two London skeletal samples used here, St. Brides and Farringdon (n=689). They found that mortality risks were significantly

higher for low status subadults, but detected little difference between the adults. The authors (DeWitte et al. 2016) suggest that either strong selective mortality operated during subadult years to result in more robust adults or the impact of healthy adult migrants arriving in London for work may have acted to decrease the mortality risks between the adults. The analysis reported here uses a much larger sample size (n=9208), but supports DeWitte et al.'s (2016) findings and also suggests that divergent survival risks, apparent across childhood and adolescence, likely resulted in a stronger selective mortality force operating on the lower socioeconomic group. Nonetheless, migration was a major force of London growth during the Industrial Revolution (Galloway 1985; Landers 1987; Landers and Mouzas 1988), so it is also possible that the arrival of healthy rural migrants may have acted to decreased mortality amongst the lower socioeconomic groups. Outward migration of people with chronic disease to their home regions may be another factor. Mortality risks derived from burial records are likely influenced by a number of factors operating during in this period, but for diseases endemic to London at this time, such as smallpox, immunologically naivety would have placed newly arrived rural migrants at heightened risk.

6.8 Adult morbidity and mortality in industrialised London

Skeletal and burial data suggest the adult environments may have differed between groups in term of morbidity and mortality risks. Males may have faced greater risks of both mortality and chronic disease, such as periodontitis. Females, however, likely risked increased exposure to certain diseases, such as smallpox and cholera. The impact of socioeconomic status is less clear, but high status St. Bride's individuals had a lower risk of severe periodontitis, as well as certain diseases including smallpox and cholera. Conversely, lower status Farringdon individuals had the greatest risk of severe

periodontitis as well as cholera and smallpox. The situation for adults from middle to high status Chelsea and middle status St. Benet's is uncertain, but they do not appear to have had a heightened or lessened risk for either periosteal new bone lesions or severe periodontal pockets.

Mortality risks could only be assessed for the two most extreme social groups, St. Bride's and Farringdon, but it is reasonable to assume that Chelsea and St. Benet's were intermediate to them. A middle socioeconomic position relative to St. Bride's and Farringdon, may explain why frequencies of health indicators tended to fall between the two extreme social groups. The similar cumulative adult survival risks of lower status Farringdon and high status St. Brides may have been influenced by selective mortality operating differentially across childhood and adolescence. Nonetheless, migration may also have shaped adult survival in contradictory ways. Healthy rural migrants may have been more robust than some individuals who were raised in London, but they were also at greater risk of morality from endemic diseases, such as smallpox. Furthermore, the relatively slower progression of tuberculosis may have resulted in many migrants who contracted the disease leaving the city, biasing mortality risks based on burials

Having investigated how the child and adult environments might have differed by group, it remains to investigate whether childhood health insults influenced adult health outcomes at an individual level.

CHAPTER SEVEN: LIFELONG LINKS BETWEEN THE CHILD AND THE ADULT

7.1 Individual associations from childhood to adulthood

The central focus of this research is whether health insults experienced in childhood influence adult health outcomes. Analysis at the individual level is now used to investigate how occurrences of childhood health insults, assessed in terms of enamel hypoplasia, might directly influence final growth outcomes, certain health conditions, as well as longevity in adulthood. First, possible associations between childhood health insults and adult femoral and tibial lengths are explored before assessment of relative risks associated with periosteal new bone and periodontitis. Finally, potential influences on survival are analysed. Relative risk analysis describes the risk, or likelihood, of an event such as death occurring before or after a point in time, given the presence or absence of certain conditions, such as a number of hypoplastic defects. The ratios describe the difference in magnitude of risks between those with and without the condition. For example, the relative risk ratio of dying after a certain age, describes the difference in risks for those with defects relative to those without defects.

Occurrences of defects are assessed in several ways, which are used in each set of analyses: the total accumulation of defects, specific thresholds in the number of defects, annual reoccurrences, and timing of defect formation. The total accumulation of defects is the total number of defects observed between two and six years (the approximate age when the mandibular canine crown has completed formation). As with the other assessments, except timing, only individuals with at least 80% of crown height remaining are included for analysis, ensuring all individuals have defects that would be observable from two years of age, from which the counts of defects begin. As it is

possible that childhood health insults might only impact later health after a certain number of episodes have occurred, specific thresholds in the number of defects present are tested. This is achieved by testing for differences in outcomes, such as age at death, between individuals with a certain number of hypoplastic defects against those with fewer. Starting with one or more defects, individuals were compared to those with no defects and for each subsequent test the number of defects tested was increased by one. In this way, a threshold should be apparent when those with more than a certain number have significantly altered outcome relative to those with fewer defects. Individuals with annually occurring defects are those with at least one defect present in each year of crown formation spanning three consecutive years, from the beginning of the second year to completion of the fourth year. The lower frequencies of defects in the fifth year did not permit reliable testing over four years. Defect timing, or the age of the individual when they experienced casual stressors, is only assessed in those who have the full complement of enamel observable for each year of age being tested; if worn crowns meant that part of the year's enamel was unobservable, they were excluded.

7.2 Childhood health and growth outcomes

7.2.1 Femoral and tibial length by age at death

Femoral and tibial lengths have been suggested to reflect childhood environments, therefore before investigating whether childhood health insults directly impacted final adult lengths, it may be useful to explore if adult lengths vary by age at death. When the groups were analysed collectively, one way ANOVA detected no significant differences between mean femoral or tibial lengths z scores and age at death (Figure 7.1). However, the youngest age group does tend to have the longer long bone

lengths. Although bone lengths did not vary by age group for males or females, they did amongst the cemetery groups. Chelsea femurs were found to differ significantly (F = 3.066, df = 3, p = 0.041). A Tukey HSD post hoc test confirmed those who died before 35 years had longer femurs, by 36.5 mm on average, than those who lived to the next age group (mean Z score difference = 1.314, SE = 0.448, p = 0.029).

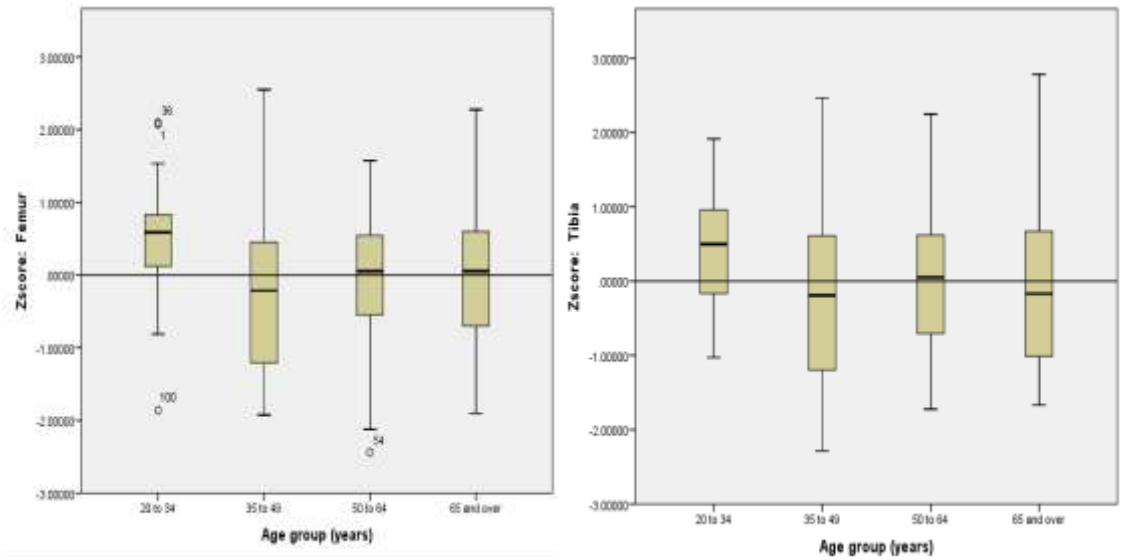

Figure 7.1 Boxplots showing Z scores for femur (left) and tibia (Right) by age at death group

As bone length in adults under 35 years appear disproportionately affected by age at death, t tests were conducted specifically on individuals who were either under or over 35 years when they died. This confirmed a significant but slight difference in mean femur lengths between those who died before 35 year of age and those who lived longer (t = 2.085, df = 88, p = 0.040). The femora of younger adults were, on average, approximately 15.5 mm longer (mean difference Z score = 0.56, SE = 0.26) than adults who lived to be 35 years or older. A similar pattern is evident in tibial lengths (Figure 7.2), but the difference did not meet the threshold for statistical significance (mean difference Z score = 0.55 (SE = 0.28), t = 1.97, df = 79, p = 0.053).

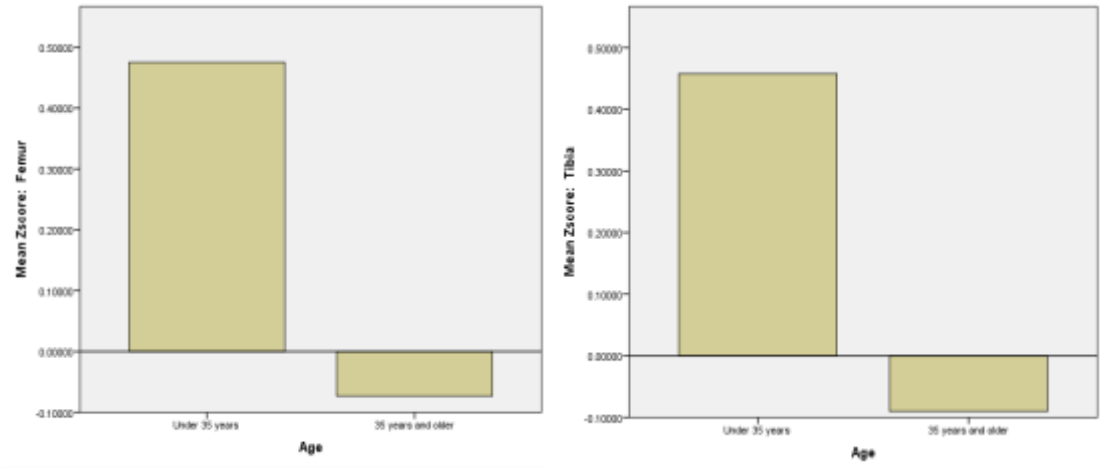

Figure 7.2 Mean Z scores femur (left) and tibia (right) for individuals under 35 or 35 years and over.

7.2.2 Femoral and tibial lengths and hypoplastic defects

Might stressful childhood episodes, reflected in hypoplastic defects, explain why adults who survived early adulthood had relatively shorter femora? Possible relationships between femoral or tibial lengths and occurrences of hypoplastic defects are investigated to understand if childhood health insults imposed a growth deficit. Pearson product moment correlation detected no significant association between the total number of hypoplastic defects per individual and either femoral or tibial lengths when groups were tested collectively (femur: R = -.089, p = 0.336, n = 118; tibia: R = -.049, p = 0.614, n =108). Similar non-significant associations were found in terms of sex and cemetery groups.

Annually reoccurring health insults were generally associated with shorter femur and tibia, but no differences were significant between those exposed or unexposed to the condition, either in terms of sex or cemetery group. When threshold effects were considered, however, it was found that femurs of adults with two or more defects were on average 13.5 mm shorter than adults with fewer defects (mean Z score

difference = -0.486, *t* = -2.454, df = 82*,p = 0.016), while no significant differences were detected for the tibia (Table 7.1). When tested by sex differences appeared to be mainly driven by females, which included both the femur and the tibia (femur mean Z score difference = -0.716, *t* = -2.961, df = 51.17 p = 0.005; tibia mean Z score difference = -0.636, *t* = -2.260, df = 42, p = 0.029). These differences equate to a mean difference in femoral length of 20 mm and tibial length of 11mm. No significant differences in bone length were detected by cemetery groups.

Table 7.1 Mean z scores and associated statistics for individuals with two or more defects (exposed) versus one or no defects (unexposed). N=count, SD= standard deviation, SE mean = standard error of the mean.

		2 or more defects	N	Z score lengths		
				Mean	SD	SE mean
Total groups	Femur	Exposed	60	-0.119	1.130	0.146
		Unexposed	30	0.366	0.732	0.134
Female	Femur	Exposed	33	-0.282	1.143	0.199
		Unexposed	21	0.433	0.629	0.137
	Tibia	Exposed	28	-0.230	0.914	0.173
		Unexposed	16	0.406	0.867	0.217

Childhood insults experienced when four and five years old may also have slightly impacted femoral or tibial lengths (Table 7.2). However depending on age, the outcomes are quite different. In general, timing of defects does not appear influential on bone length in terms of cemetery groups, but females who experienced health insults when four years of age have femurs 14 mm shorter, on average, than females who did not have defects at this age (mean difference Z score = -0.619, t = -2.473, df = 62, p = 0.016), while males were not significantly affected. The only other significant difference occurred when all groups were collectively analysed. Individuals who had

defects when five years of age had tibia that were 20 mm longer, on average, than those who did not experienced insults at this age (mean difference Z score = 0.815, t = 2.131, df = 106, p = 0.035). Although the result is surprising, the probability value is only suggestive due to the small number of exposed individuals.

Table 7.2 Mean z scores and associated statistics for femoral lengths of females exposed and unexposed to defects when 4 years and tibial lengths for collective sample exposed and unexposed to defects when 5 years old. N=count, SD= standard deviation, SE mean = standard error of the mean.

			Z score lengths			
			n	Mean	Std. Dev.	SE mean
4 years old: 1 or more defect	Female Femur	Exposed	23	-0.397	1.039	0.216
		Unexposed	41	0.223	0.916	0.143
5 years old: 1 or more defect	Total groups Tibia	Exposed	7	0.763	0.866	0.327
		Unexposed	101	-0.053	0.985	0.098

7.2.3 Impacts of childhood health on final femoral and tibial lengths

If we assume that final femoral length is reflective of the developmental environment, it seems contrary to expectations that their lengths were longer in adults who died before they reached 35 years of age. The difference in bone lengths is subtle, but suggests those who died as younger adults may have experienced less stressful development environments than those who lived longer. Occurrences of hypoplastic defects are associated with an increased likelihood of having shorter bone lengths, with the femur particularly impacted, and explains this particular paradox. Adults who had experienced multiple health insults between two and six years of age tended to have shorter femurs in general than adults who had fewer childhood insults. The association was most marked in females where both the femur and tibia where affected. Females

were also more likely to have shorter femur if they had health insults when they were four years old. In contrast, a general relationship between health insults when five years old was noted but appeared associated with longer tibia. It seems unlikely that an insult at a specific age would elicit increased tibial growth. As the result is at odds with other outcomes, it may represent a type I error. While occurrences of hypoplastic defects may explain the shorter bone lengths, it doesn't address why individuals with multiple childhood insults appear more robust as adults compared to individuals with evidence of fewer insults. Measures of adverse health experienced in adulthood may provide further insight.

7.3 Childhood health and adult morbidity risks

Childhood health insults are associated with growth deficits that may have influenced final adult height, particularly in females, but might they also have influenced adult morbidity in term of periosteal new bone and periodontitis? I investigate whether the number of childhood health insults, their annual recurrences, or age when they were experienced might be associated with periosteal new bone or periodontitis in adulthood.

Contingency tables (2x2) were constructed that distinguish between individuals with three or more defects against those with fewer, those either with or without annual defects, as well as the presence or absence of defects in each year of age. Individuals exposed and unexposed to these conditions are tested for their relative risk for periosteal new bone lesions and periodontal pockets. Periodontal pockets, as opposed to lesions indicative of chronic periodontitis, were chosen as these represent a more severe form of periodontitis, which was also suggested to be less age related. Chi square tests

are used to identify associations between the four contingencies that are unlikely to occur by chance. For cells where observed frequencies differ significantly to that expected by chance, the relative risk of acquiring the state, or not, is calculated for those who were exposed and unexposed to childhood insults.

7.3.1 Periosteal new bone formation

No significant associations were found between active or mixed periosteal new bone formation and having any defect condition. However, the probability of healed lesions may have been increased for Chelsea individuals if they had a least three defects (Table 7.3). This suggested 33% of individuals exposed to three or more serious childhood health insults acquired healed periosteal new bone lesions compare to 6.2% of the unexposed group. No other forms of periosteal new bone were found to produce significant risk associations. Neither defects occurring annually nor age at formation were found to associate with adult risks of periosteal new bone. Therefore, with the possible exception of Chelsea, it appears that childhood stressors are not particularly linked to increased adult risks of periosteal new bone.

Table 7.3 Frequencies of Chelsea individuals exposed and unexposed to three or more defects and the presence or absence of healed periosteal new bone lesions. α=0.012. Exact sig. =Fisher's exact significance. RR = relative risk. CI = confidence interval.

		Periosteal new bone: healed				
		Present	Absent	n	Exact sig.	RR (95% CI)
Three or more defects:						
Chelsea	Exposed	33.3%	66.7%	12	0.039	5.33
	Unexposed	6.2%	93.8%	32		(1.12-25.44)

7.3.2 Periodontitis

In contrast to periosteal new bone lesions, occurrences of defects were found to be clearly associated with risks of severe periodontitis in adulthood, specifically when 25% or more of observable septa are affected by pocket lesions. Although this effect is evident when groups are analysed collectively, it is males and individuals from Farringdon who were the most impacted (Table 7.4). The number of defects did not have any detectable impact on periodontal pockets, but annually occurring ones as well as their timing were found to significantly impact risks of severe periodontitis.

In general, individuals with annual childhood health episodes were five times more likely to have periodontal pockets as adults (Table 7.4). Further, males were at six times the risk of pockets if they had experienced annual health insults, but females were not affected. When cemetery groups were tested, only Farringdon individuals were found to have a significant association between annual defects and periodontal pockets.

Table 7.4 Frequencies of groups exposed and unexposed to occurrences of defects and periodontal pockets (at least 25% of observable septa affected). Sig. = exact significance. RR= risk ratio.

		Periodontal pockets				
		Present	Absent	n	Sig.	RR (95% CI)
Annual defects:						
Total groups	Exposed	40.0%	60.0%	20	0.001	5.067 (2.220-11.566)
	Unexposed	7.9%	92.1%	114		
Male	Exposed	61.5%	38.5%	13	<0.001	6.154 (2.413-15.691)
	Unexposed	10.0%	90.0%	50		
Farringdon	Exposed	57.1%	42.9%	7	0.006	13.143 (1.741-99.21)
	Unexposed	4.3%	95.7%	23		
Defects at 2 years:						
Males	Exposed	34.5%	65.5%	29	0.026	3.908 (1.187-12.863)
	Unexposed	8.8%	91.2%	34		
Farringdon	Exposed	41.7%	58.3%	12	0.006	0.583* (0.362-0.941)
	Unexposed	0.0%	100.0%	18		
Defects at 4 years:						
Total	Exposed	25.0%	75.0%	68	0.022	2.208 (1.126-4.330)
	Unexposed	11.3%	88.7%	106		
Farringdon	Exposed	45.0%	55.0%	20	0.033	2.813 (1.014-7.804)
	Unexposed	16.0%	84.0%	25		
Defects at 5 years:						
Total groups	Exposed	38.5%	61.5%	13	0.044	2.580 (1.182-5.631)
	Unexposed	14.9%	85.1%	161		

**Risk ratio for individual without defects (ratios could not be calculated for those with defects at two years as none occurred)*

Timing was also significant. Defects that formed when males or Farringdon individuals were two years of age were associated with an increased risk of pockets. A threefold increase in risk of severe periodontitis was suggested for males, while for Farringdon individuals who lacked defects at two years, their risk of pockets was halved. Defects occurring at four and five years of age, but not three years, doubled

the risk of pockets collectively, while of the cemetery groups, again only Farringdon was impact by defects occurring when four years old.

It is apparent that occurrences of hypoplastic defects are associated with severe periodontitis in adulthood in certain situations, but it is uncertain whether this relationship is direct or reflects factors such as correlated environments or selective mortality. Considering how occurrences of hypoplastic defects might also impact adult survival may elucidate these life course connections and whether childhood health insults may have influenced differential levels of frailty in adulthood.

7.4 Childhood health and adult survival

Although morbidity indicators such as periosteal new bones lesions and severe periodontitis are valuable in providing more subtle insight into adult health, age at death is the most convincing gauge of health outcomes. How childhood insults may have influenced adult longevity is perhaps the most definitive indicator of how early life effects may carry across the life course, particularly when analysing dental and skeletal data.

7.4.1 Accumulation of childhood health insults

The following analysis is undertaken to understand how the total number of defects an individual accumulated in childhood might impact adult health risks. The frequencies of defect numbers are displayed in Table 7.5. In all groups, the most common number of defects, or health insults that caused defects to form, was two. Fourteen individuals had no defects, while four had a maximum of five.

Table 7.5 The number of hypoplastic defects per individual and their frequencies by group.

		Numbers of hypoplastic defects per individual						Total n
		0	1	2	3	4	5	
Males	%	6.1%	19.7%	37.9%	22.7%	7.6%	6.1%	
	n	4	13	25	15	5	4	66
Female	%	13%	24.7%	37.7%	18.2%	6.5%	0%	
	n	10	19	29	14	5	0	77
St. Bride's	%	2.9%	26.5%	41.2%	17.6%	8.8%	2.9%	
	n	1	9	14	6	3	1	34
Chelsea	%	9.1%	34.1%	29.5%	22.7%	4.5%	0%	
	n	4	15	13	10	2	0	44
St. Benet's	%	12.1%	9.1%	45.5%	18.2%	6.1%	9.1%	
	n	4	3	15	6	2	3	33
Farringdon	%	15.2%	15.2%	36.4%	21.2%	12.1%	0	
	n	5	5	12	7	4	0	33
Total	%	9.7%	22.2%	37.5%	20.1%	7.6%	2.8%	
	n	14	32	54	29	11	4	144

The number of insults that occurred between two and six years of age does not appear strongly related to age at death for these individuals who survived to adulthood. If anything, in certain situations childhood insults appear slightly advantageous to living longer. Overall, Spearman's correlation coefficient suggests no significant associations exist between the total number of defects and age at death ($R_S = 0.117$, $p = 0.162$, $n = 144$). There was also no difference when sexes were considered separately (male $R_S = 0.213$, $p = 0.087$, $n = 66$; females $R_S = 0.005$, $p = 0.967$, $n = 77$)

While a similar outcome was found for most of the cemetery groups, a slight positive association was suggested for St. Bride's ($R_S=0.373$, $p=0.030$, $n=34$, explaining about 14% of the variation (Figure 7.3). While no other associations were detected between the number of defects and age at death, it is apparent from the distributions that

for those who survived to adulthood, incurring multiple childhood defects did not create a particular barrier to reaching older ages.

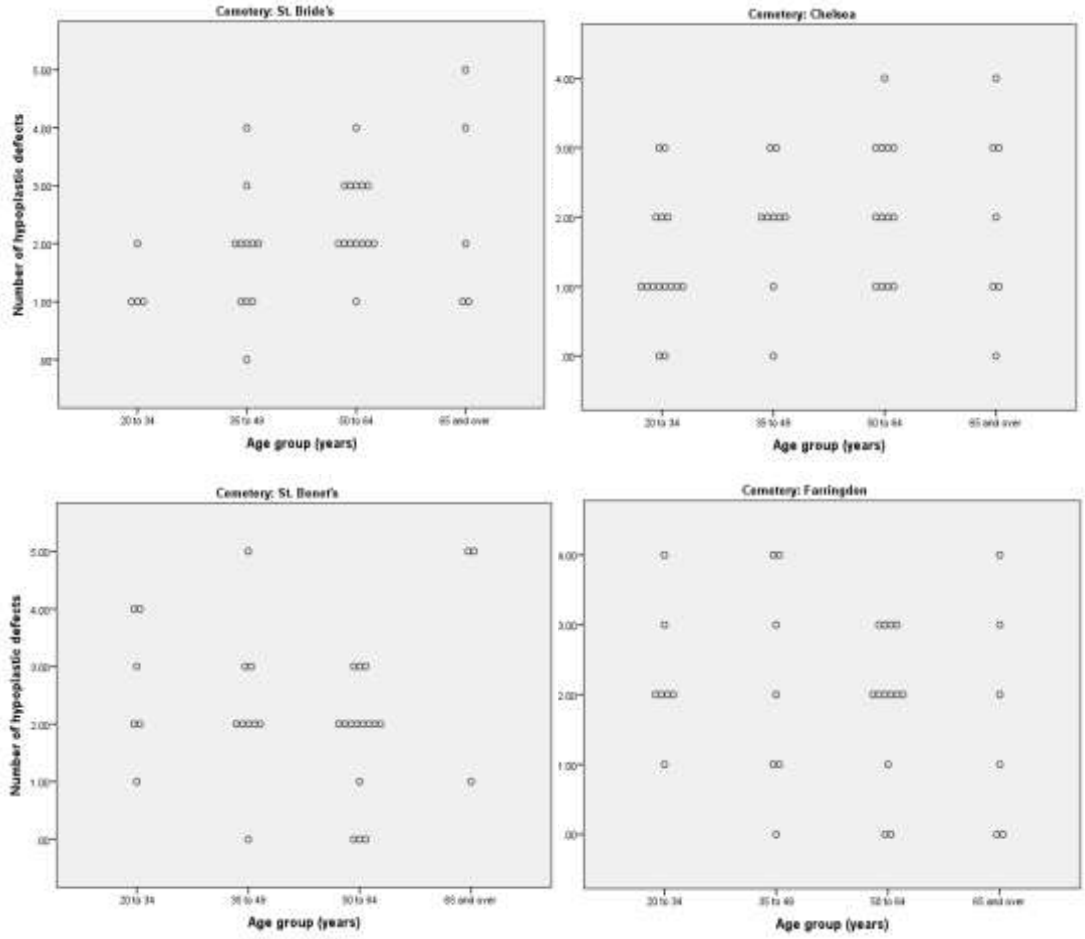

Figure 7.3 Scatterplots for cemetery groups showing association between age at death and number of hypoplastic defects. Only St. Brides (top left) showed a significant (positive) correlation.

7.4.2 Threshold effects

In these samples, the accumulation of childhood insults experienced between two and six years of age does not appear detrimental to adult survival. However, it may be useful to know if a threshold effect was operating where the impact on longevity might shift when the number of defects is above or below a certain quantity. Kaplan-Meier survival analysis is used to assess the overall cumulative impact on survival

across adulthood as well as relative risk used to target age specific impacts. To detect if age groups are disproportionately impacted, individuals are classified as either younger or older than 35, 50, and 65 years at death with their mortality risk providing a measure of the likelihood of either dying before or surviving past each age threshold. This two tiered approach is used because the log rank test, used in Kaplan-Meier survival analysis, assumes that the risk of death is proportional across the ages being assessed. However, as the age groups used here are broad (approximately 15 years) and span adulthood, this assumption may not be met. For example, if mortality risks for a certain condition are pronounced in early adulthood, but diminish in older ages, age specific relative risks may be able to detect the shift. Kaplan-Meier analysis, on the other hand, can inform on risks where cumulative differences span across adulthood.

When cumulative survival (Kaplan-Meier) is analysed with all samples as a single collective group, no specific number of defects appear to influence the likelihood of survival over adulthood. Analyses conducted in terms of sex, however, suggest male survival appears to show a threshold effect. As shown in Table 24 and Figure 7.4, males with at least three defects have a significantly higher chance of survival ($p = 0.046$), which equates to approximately six years increased survival time over adulthood. Although this is not below the Bonferroni adjusted alpha level ($\alpha = 0.012$), a threshold is also indicated among males with four or more insults during childhood, Table 7.6 and Figure 7.5. Despite the smaller sample size in the second assessment (four or more defects), it supports the result of the first test (three or more defects), suggesting the higher probability value does not indicate a type I error. Therefore, some males may have experienced increased survival if they experienced multiple insults as children. Alternatively, males who experienced fewer insults suffered decreased adult survival.

Table 7.6 Significantly different Kaplan-Meier survival curves between males with total of 2 or less defects versus 3 or more and for 3 or less versus 4 or more. Mean survival time is based on age groups which cover approximately 15 years, i.e. age group 1 is from 20 to 34 years, age group 2 is from 35 to 49 years etc.

	Males		Males	
Defect number	2 or fewer	3 or more	3 or fewer	4 or more
Mean survival time	2.52	2.96	2.58	3.33
95% CI	2.26-2.78	2.58-3.32	2.36-2.80	2.68-3.99
n	42	24	57	9
Log Rank	X^2 =3.99, df = 1, p = 0.046		X^2 =7.21, df = 1, p = 0.007	

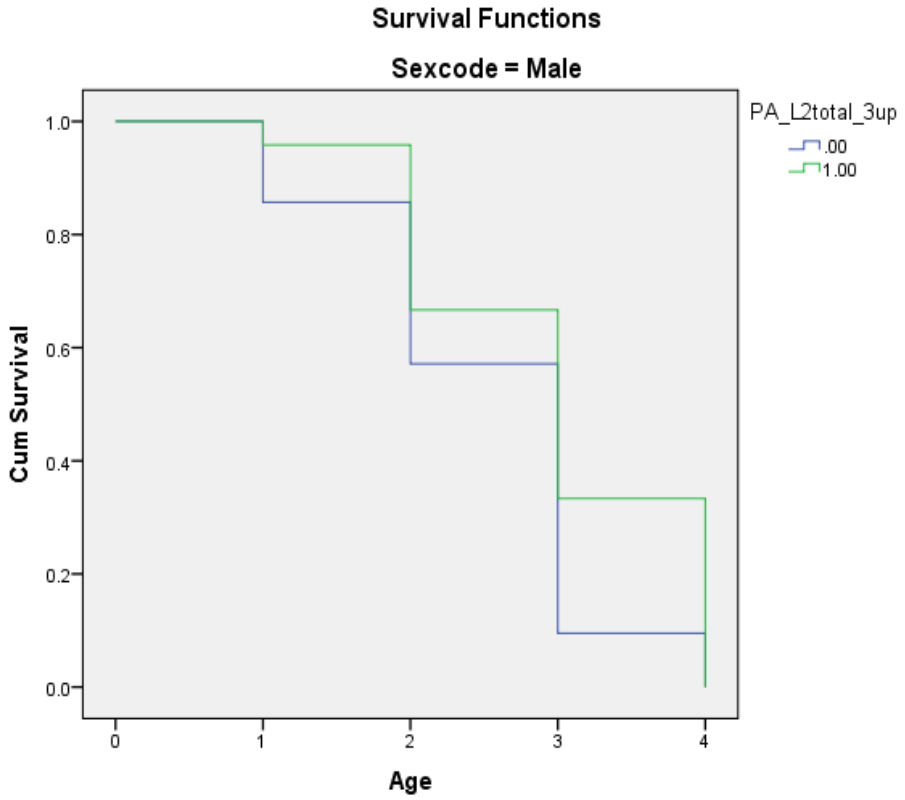

Figure 7.4 Kaplan-Meier survival curves for males with 3 or more defects (green line) versus males with fewer (blue line).

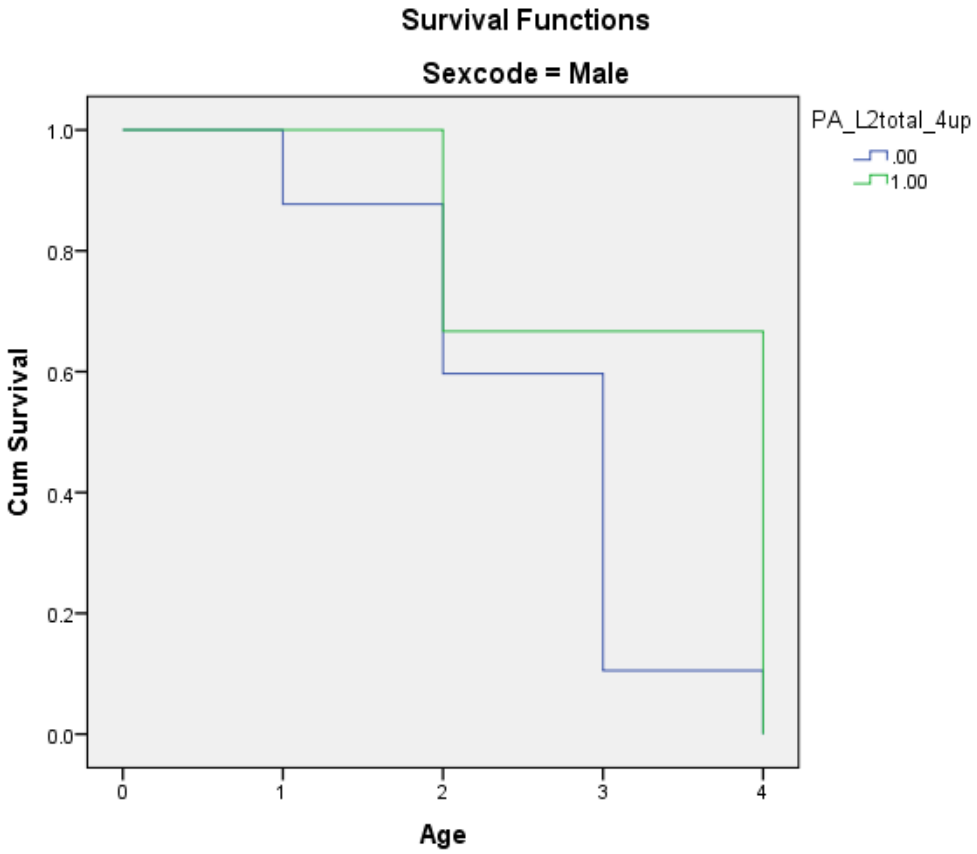

Figure 7.5 Kaplan-Meier survival curves for males with 4 or more (green line) versus fewer (blue line).

However, the relative risks of mortality were not always consistent across adulthood. As referring to the relative risk of survival is counter intuitive, risk ratios that refer to the risk of death after a certain age are referred to as the likelihood of survival, while risks ratios that describe the likelihood of death before a certain age are referred to as mortality risks. Both ratios are used in distinct analyses dependent upon the nature of the data.

In this analysis, age specific relative risk ratios suggest that when groups are assessed collectively there is a significantly decreased mortality risk prior to 35 years for individuals with more than two defects, Table 7.7 ($X^2 = 4.219$, df = 1, p = 0.040). This points to mortality risks in the younger adults as being particularly acute compared to older ages. The relative risk ratio suggests that those who were exposed to at least

two childhood health insults had nearly half the risk of dying before 35 years as individuals who experienced fewer. The confidence intervals associated with older ages, 50 and 65 year thresholds, include '1', so the likelihood of no difference between exposed and unexposed groups cannot be excluded.

Table 7.7 Relative risk of mortality and confidence intervals for total groups with two or more defects for specific age thresholds. Significant confidence intervals (CI) are bolded.

Total groups	Mortality prior	35 years	50 years	65 years
Two or more defects	RR 95% CI n=144	**0.532** **0.292-0.969**	0.807 0.571-1.142	1.091 0.929-1.281

As suggested by Kaplan-Meier analysis, males with three or more defects experienced a cumulative increase in survival across adulthood, but relative risk ratios suggest the likelihood of survival was largely confined to older ages (Table 7.8). Males were three and a half times more likely to survive past 65 years if they had at least three defects. This association was again strengthened when four or more defects were considered.

Table 7.8 Likelihood of survival and confidence intervals for males with three or more and four or more defects for specific age thresholds. Significant confidence intervals (CI) are bolded.

Male	Survival past:	35 years	50 years	65 years
Three or more defects	RR 95% CI n=66	1.118 0.963-1.298	1.167 0.793-1.715	**3.500** **1.176-10.414**
Four or more defects	RR 95% CI n=66	**1.140** **1.034-1.256**	1.118 0.672-1.859	**6.333** **2.609-15.372**

Of the cemetery groups, only survival of Chelsea individuals appear significantly impacted by the number of defects (Table 7.9). For this group, having two or more defects meant they were 1.7 times more likely of surviving past 35 years than those with fewer defects (X^2=5.116, df=1, p=0.024). This survival effect was limited to the youngest age group.

Table 7.9 Likelihood of survival and confidence intervals for Chelsea individuals with two or more defects for specific age thresholds.

Chelsea survival past:	35 years	50 years	65 years
Two or more defects			
RR	**1.689**	1.411	1.013
95% CI	**1.011-2.821**	0.702-2.839	0.257-4.000
N	**44**	44	44

Threshold effects are evident amongst males and middle to high status Chelsea, but suggest the number of childhood health insults required to elicit a response may vary slightly depending on the group in question. In addition, whether the effect is most evident in early or later adulthood can also shift. This emphasised how factors influencing adult health outcomes might vary both by sex and cemetery group. As this response was only evident in one cemetery group, rather than a graded response reflecting varying socioeconomic positions, the groups may differ in additional ways, such as the proportion of migrants represented in each cemetery groups. Potentially confounding influences, such as migration, will need to be considered when interpreting results.

Variation in the number of childhood health insults associated with different thresholds suggest that life course effects might only be apparent after a certain number of stressors were experienced. This could suggest that childhood stressors need to

accumulate to a certain level before a long term effect is realised. Except, however, the total accumulation of childhood insults between two and six years only impacted the higher status group, which was beneficial to survival. This is the opposite to what would be expected from an accumulation of stressors causing physiological damage. It is also possible the repetition of health insults is connected to later life health outcomes, such as would be evident as annually occurring hypoplastic defects.

7.4.3 Annually repeated health insults

The impact that repeated childhood health insults might have on adult survival is investigated by analysing individuals with hypoplastic defects occurring annually over three continuous years. Frequencies of individuals with annual occurrences starting from two years of age are displayed in Table 7.10. These were more frequent in males than females, while among the cemetery groups Farringdon had the most and Chelsea the least (significance is discussed in conjunction with relative risk, after cumulative survival differences).

Table 7.10 Frequencies of individuals with defects formed each year from beginning of second years to completion of fourth year.

	Annually occurring defects						
	Male	Female	St. Bride's	Chelsea	St. Benet's	Farringdon	Total
%	19.7%	7.8%	14.7%	9.1%	12.1%	21.2%	13.9%
n	13	6	5	4	4	7	20

Collectively, the Kaplan-Meier survival curves did not differ significantly between those with annually occurring defects and those without. While neither females nor the cemetery groups showed significant differences in cumulative survival, a suggestive result was detected for males (Figure 7.6). Males with annually occurring

health insults were more likely to have increased survival relative to males without, with an increased survival time of approximately eight years (Table 7.11). However, caution is required in interpreting these results as it is possible the differences in survival reflect the quantity of defects rather than their regularity as individuals who meet the criteria of having annually occurring defects over four years must also have accumulated a minimum of three defects.

Table 7.11 Kaplan-Meier survival curves between males with and without annual defects, including Log rank (Mantel-Cox) test. Mean survival time is based on age groups which cover approximately 15 years, i.e. age group 1 is from 20 to 34 years, age group 2 is from 35 to 49 years etc.

	Annual defects	
Males	Present	Absent
Mean survival time	3.15	2.57
95% CI	2.72-3.59	2.33-2.80
N	13	53
Log Rank	X^2 =4.28, df = 1, p =0.039	

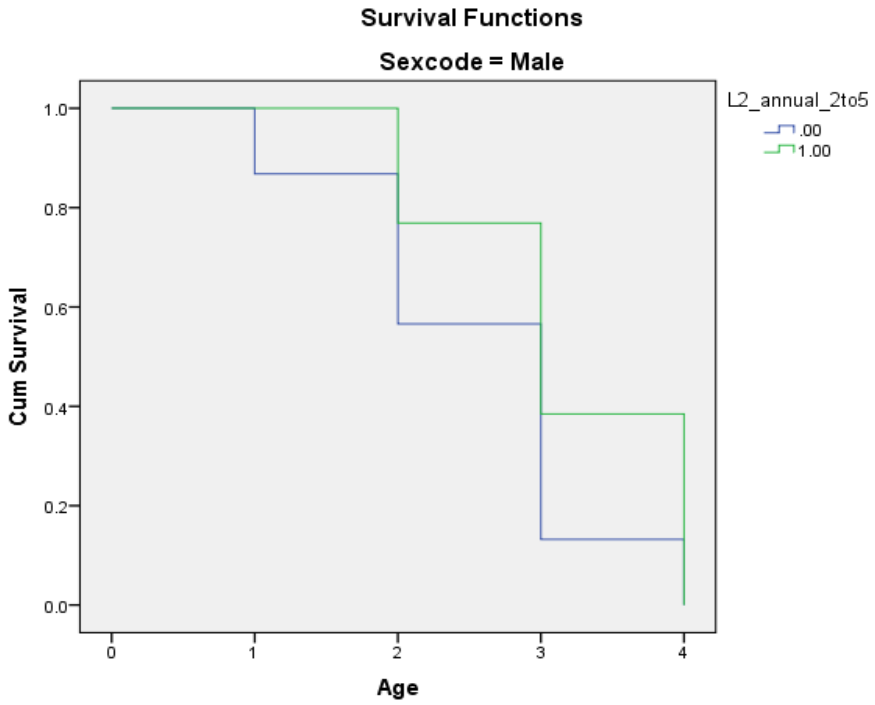

Figure 7.6 Kaplan-Meier curves for males with annual defects (1) verse males without (0).

The relative risk of annual health insults also varied by sex, but not cemetery group (Fisher-Freeman-Halton exact, p = 0.515). Males were significantly more likely than females to have annual defects ($X^2 = 4.372$, df = 1, p = 0.037), with those exposed 1.6 (95% CI = 1.109-2.311) times more likely to be male. The likelihood of male survival also varied across the age groups, with a slightly greater chance of surviving past 35 years, but nearly three times as likely to survive past 65 years (Table 7.12). These relative risk ratios, however, are not as high as those associated with having at least three or four defects. This suggests relative risk ratios associated with annual occurrences may in fact be reflecting increased survival associated with males who accumulated at least three defects.

Table 7.12 Male likelihood of survival for those exposed to annual defect compared to males without exposure

Annual defects survival past:	35 years	50 years	65 years
Males			
RR	**1.152**	1.359	**2.912**
95% CI	**1.037-1.280**	0.930-1.987	**1.099-7.714**
n	**66**	66	**66**

7.4.4 Timing of childhood health insults

The influence that the timing of childhood health insults, experienced between two and six years, might have on adult survival is now investigated. The frequencies of defects occurring in specific age ranges are displayed in Table 7.13. The most common age for defects to occur was during the third year, regardless of group membership.

Table 7.13 Frequencies of individuals with defects (1 or more) formed at specific ages. Percentages based on number of individuals with crown region observable for each age range (N observable).

Age		Male	Female	St. Bride's	Chelsea	St. Benet's	Farringdon	Total
2 -2.99	%	43.9%	36.4%	52.9%	31.8%	39.4%	39.4%	40.3%
	n (defects)	29	28	18	14	13	13	58
	N observable	66	77	34	44	33	33	144
3-3.99	%	78.4%	71.4%	7.6%	71.2%	82.2%	73.5%	75.3%
	n (defects)	80	65	31	42	37	36	146
	N observable	102	91	41	59	45	49	194
4-4.99	%	58.5%	29.7%	39.0%	32.2%	46.7%	44.0%	40.0%
	n (defects)	50	27	16	19	21	22	78
	N observable	103	91	41	59	45	50	195
5-5.99	%	9.7%	5.5%	4.9%	8.5%	8.9%	8.0%	7.7%
	n (defects)	10	5	2	5	4	4	15
	N observable	103	91	41	59	45	50	195

The timing of childhood health insults did not have a significant impact of survival, for any group. Males were found to be significantly more likely (RR=1.433, 95% CI 1.107-1.855) to have defects when four years old compared to females (X^2=7.190,df=1, p=0.007), but the age specific risks for exposed and unexposed did not differ significantly. So although males may have experienced more defects at this age, the insults do not appear to have influenced adult health outcome.

7.5 Lifelong health connections

These analyses investigated how childhood health insults impacted adult health outcomes at an individual level, allowing a more detailed, or personalised, investigation than was possible using only group level assessments. These results are now discussed in terms of immediate patterns and associations that were evident in the data before considering their relevance within a broader life course framework in the following chapter.

For those who survived to adulthood, neither the total number of health insults experienced between two to six years of age, nor ages within this range, appear detrimental to adult longevity. For some individuals experiencing more childhood insults may have been beneficial to adult survival. While a beneficial association between hypoplastic defects and survival is uncommon in bioarchaeological studies, it is not unknown. For example, in an analysis of enamel hypoplasia in a Barbados slave population, Corruccini et al. (1985) reported individuals with no defects died earlier in adulthood than those with defects. More recent work focused on the Irish potato famine found children with more defects were found to survive longer than children who had fewer (Geber 2014). The author suggests that children who had experienced fewer health insults may have been frailer due to immunological naivety resulting from fewer previous exposures to infectious disease, which was the main cause of death for many of these children (Geber 2014). A study assessing health insults in medieval Demark used pathological features of internal enamel (accentuated striae) to gauge physiological stress (Gamble et al. 2017). Increasing levels of childhood stress was associated with increased survival in adult females, but not males (Gamble et al. 2017). In this research, for some individuals from high status St. Bride's the more childhood health insults they had experienced, the longer they were likely to live as adults. While for middle to high status Chelsea individuals their risk of death before 35 years was nearly halved if they had at least two childhood insults. Collectively, there is also a reduced risk of dying before 35 years for individuals who experienced multiple health insults. Males were more likely to survive to the oldest ages if they had a least three childhood insults, an association that was strengthened if they had experienced four or more insults. It is important to consider that it may not be the precise number of hypoplastic defects that are important, but rather the varying likelihood of childhood exposures they represent.

Significant associations also exist between exposure to childhood insults and adult likelihood of periosteal new bone lesions and severe periodontitis. The link with periosteal new bone lesion was only evident for middle to high status Chelsea individuals, who were more likely to have healed periosteal lesions if they had experienced at least three childhood insults. Work by DeWitte (2014), suggests that healed periosteal new bone lesions may be an indicator of survival, which again could imply a positive influence on longevity for higher status individuals with more than the average number of defects.

One of the few situations where the timing of childhood health insults appears relevant is also with increased risks of severe periodontitis. A general, or collective, increased risk was linked to health insults experienced when four and five years old, but Farringdon individuals where at particular risk from insults at four years of age. Males experienced an increased risk of severe periodontitis if they had health insults when two years. As annual occurring insults also increased the risk of severe periodontitis for the same groups (collectively, males, and Farringdon), it is unclear whether it is the repetition of adverse health episodes or their timing that is relevant. However, the risks associated with annual occurrences were consistently greater, suggesting that it is the regular episodes of adverse health that is more indicative of adult health outcomes, while timing may be largely incidental.

In general, individuals with multiple defects were more likely to have shorter femora, but also more likely to live past 35 years. This relationship is evident in Figure 7.7, where the longest femurs, on average, are found in individuals who died before 35 years and who have either one or no hypoplastic defects. In contrast, individuals with the shortest femurs are 35 years or older and have at least two defects. This effect was particularly marked in Chelsea individuals. Insults timing may also have impacted

femur length. Although females were more likely to have both shorter femur and tibia if they had more than two health insults, they were also likely to have shorter femur if they experienced adverse health when they were four years old. Conversely, when groups were assessed collectively, longer tibia were associated with health insults that occurred when five years old but it is difficult to establish if this result is meaningful as it stands apart to the general trends observed in the samples.

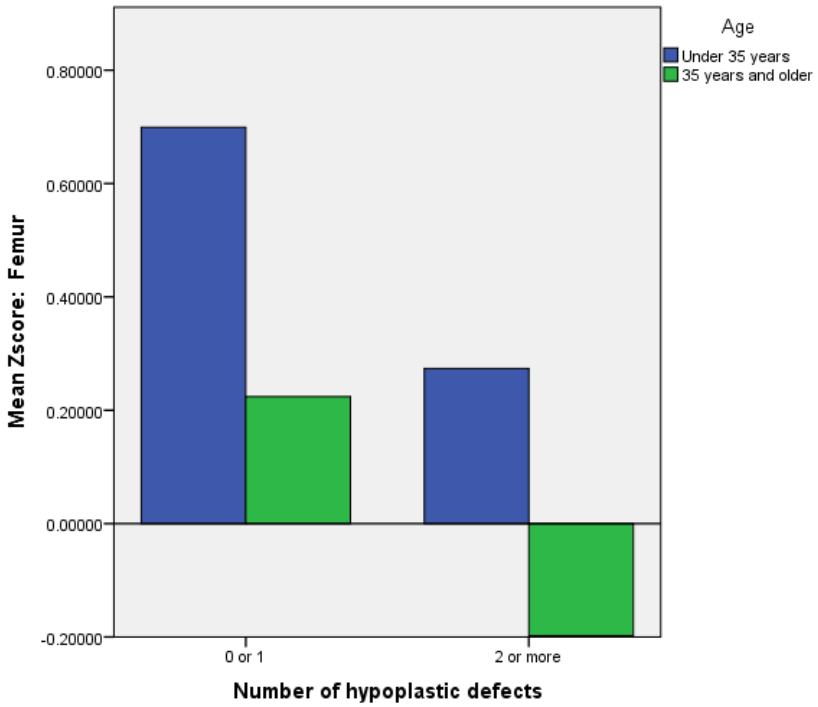

Figure 7.7 Femur Z scores for individuals with none or one hypoplastic defect compared to those with more and who died before 35 years of age or survived longer.

Over all, these results suggest that there are lifelong associations between childhood health experiences and adult health outcomes but not necessarily in the way that might be assumed. In some situations, experiencing fewer childhood health insults may be more detrimental to adult survival than having experienced a greater number. However, adverse health in childhood still incurred a cost, evident as either growth deficits or an increased likelihood of severe periodontitis in adulthood. These results

will be considered within a life course framework to identify mechanisms that might explain how these early and later health outcomes are connected. Mechanisms that may be influencing frequencies of stress indicators in adults who survived childhood, such as selective mortality, scarring, or correlated environments are discussed in light of the changing landscape of London's urbanisation.

CHAPTER EIGHT: HOW MIGHT CHILDHOOD STRESSORS INFLUENCE ADULT HEALTH?

8.1 Do childhood stressors impact adult health?

The central question of this thesis concerns the circumstances when childhood health experiences might alter adult health outcomes? To address this question, I extended information derived from human remains with historical research to provide a fuller context in which to interpret the skeletal evidence. The outcomes suggest that adverse health experienced after the age of two can carry a cost extending into adulthood. However, the price and the specific hazard differ depending on one's sex or socioeconomic position. This discussion begins with considering how physiological insults in childhood appear to directly impact adults in general and then how risks and impacts can shift depending on sex and socioeconomic status.

8.2 General impacts of early health insults

When all individuals who survived to adulthood are considered as a single group, the only detectable impact of multiple childhood health insults on adult longevity is beneficial. Furthermore, the adults appear to fall into two distinct groups: those who experienced only one or lacked any childhood health insults and were more likely to die before 35 years of age as well as have longer femora. The group who experienced multiple childhood health insults were less likely to die as younger adults but have shorter femora, suggesting that childhood health insults incurred a growth cost. Using the risk direction model proposed by Preston et al. (1998) to guide interpretation (Figure 8.1), when higher risks of adversity in childhood, evident as having experienced

relatively more health insults, connect to a lower adversity risk in adulthood, or increased survival, it describes a negative direction of risks. According to Preston et al. (1998) this could point to either acquired immunity or selective mortality as mechanisms underlying this life course association. Neither of these, however, would explain the counter group who have fewer early insults and shorter adult life, but the process of immunological naivety might serve as an explanation.

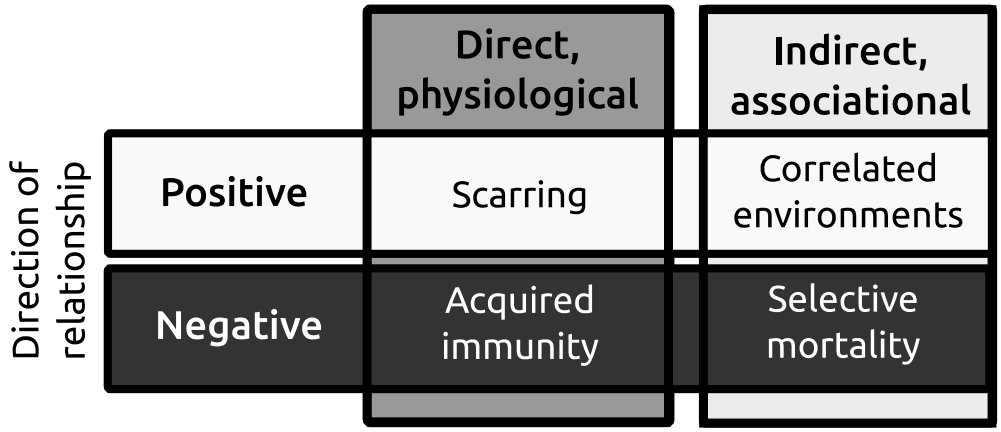

Figure 8.1 Direction of risk relationships between risks in childhood and adulthood (adapted from Preston et al. 1998)

Operating as the inverse of acquired immunity, individuals who lacked exposure to certain infectious pathogens in childhood may be placed at greater risk of mortality if they then encountered these infections when older, for example, in early adulthood. In the skeletal record this will be evident as a younger age of death among individuals with fewer enamel defects, as reported in work by Geber (2014) on the Irish Potato famine victims. If immunological naivety explains the relationship between fewer childhood health insults, longer femora and dying in early adulthood, then acquired immunity is possibly driving the life course association observed in those who experienced multiple childhood insults and were more likely to live longer. Work that utilised American Civil War data to explore factors influencing mortality risks amongst

soldiers found that those from rural backgrounds experienced increased mortality risks during conscription, despite being from apparently healthier environments (Lee 1997). More of these soldiers died from diseases that infer long term immunity, such as smallpox, compared to soldiers from urban backgrounds (Lee 1997). The author explains that soldiers from urban backgrounds probably had immunity to many of these diseases, while the rural recruit were more likely to be immunologically naive.

Annually occurring childhood health insults were found to be a risk factors for chronic morbidities in adulthood, specifically severe periodontitis. This relationship shows a positive risk direction, suggesting either direct physiological scarring or indirect correlated environments. It would seem unlikely that periodontitis, which is an oral bacterial infection affecting adults (Armitage 2004; Cochran 2008), would result from physiological scarring caused by childhood health insults. However, research has suggested a link between higher rates of periodontitis in adults who grew up in lower socioeconomic circumstances, which persisted even among those whose were upwardly mobile as adults (Poulton et al. 2002). What is unclear is why repeated insults would be connected to adult morbidity, but not the total number of stressors experienced. It is possible that childhood environments in which regular annual childhood health insults were more common were similar to environments experienced in adulthood. For example, respiratory viruses such as respiratory syncytial virus and para-influenza virus are responsible for many acute lower respiratory infections in infants and children, including pneumonia and bronchitis and are more common in lower socioeconomic communities. (Ran Kim et al. 2000). These have a high rate of annual reinfection as acquired immunity is neither complete nor long lasting (Hall et al. 1991; Hall 2001). In addition, periodontitis is often more frequent among lower socioeconomic status adults, because of risk factors such as chronic disease and smoking (Grossi et al., 1995; Li et

al. 2000; Sharma et al. 2016), as well as psycho-social stresses and poor nutrition (Clarke and Hirsch 1995).These studies support the suggestion that the link between annual childhood health insults and severe periodontitis in adulthood might reflect correlated environments.

Results demonstrate how tangled and potentially paradoxical the relationship between childhood experiences and adult health outcomes can be, particularly when using bioarchaeological analyses. Furthermore, when the sample is analysed in terms of sex, it is not only apparent that risks vary between the sexes, but that mechanisms maintaining relationships between early and later life also differ depending on whether adversity risks are assessed within or between males and females.

8.3 Male and female variation in risks and impacts over the life course

8.3.1 Male health insults and survival

Among males, those who experienced at least three childhood health insults (as reflected in enamel hypoplasia) were more likely to survive past 65 years compared to males with fewer health insults. The direction of adversity risks for males suggests a negative association; higher adversity risks in childhood linked to a lower adversity risk in adulthood. Again this could point to either acquired immunity or selective mortality, depending whether the risks reflect direct physiological damage or indirect associational influences, such as selective mortality. Considering how mortality risks might vary over the life course may help explain this variation and suggest whether selective mortality is a likely explanation for males.

Mortality risks determined from parish burial records, suggest that from birth to nineteen years of age, the chance of survival did not differ markedly between males and

females, but did over the course of adulthood. Males faced a generally greater risk of death than females, which became more marked after 35 years, but was most acute around 60 years. This could support selective mortality operating on males over adulthood where only the more robust (who had survived multiple childhood health insults), entered the oldest age group. This situation is evident in other work where individuals who experienced higher levels of early stressors lived longer in adulthood than those who had experienced lower levels (Preston et al.1998; Crimmins 2005; Eberstein et al.2008; Costa 2012). The influence of selective mortality is often evident as cross-over mortality in age at death profiles, where after a certain age individuals with evidence of relatively more early insults may have an increased likelihood of survival than those with fewer (Crimmins 2005; Quaranta 2014). A similar pattern was noted in American Civil War prisoners who survived incarceration, revealing that differential levels of frailty existed within the group, but which only become apparent in old age (Costa 2012)

8.3.2 Variation in survival between males and females

When males and females are compared, as opposed to comparisons only within males, the direction of life course risks are positive for each, suggesting either scarring or correlated environments as mechanisms. Females have a lower risk of childhood insults, on average, along with a lower mortality risk in adulthood, based on burial records. In contrast, males have an increased risk of childhood insults and an increased risk of death in adulthood, suggesting that childhood health insults may disadvantage adult survival. A similar pattern is evident in adults from medieval Demark, where females had general lower levels of stress (evidenced by pathological striae in the internal enamel) than males (Gamble et al. 2017). However, in males increased stress

was associated with decreased survival, but in females it was associated with increased longevity (Gamble et al. 2017). In this research, although males also show generally decreased adult survival with higher numbers of defects, paradoxically, within males it is those with more defects that are likely to have increased survival.

The risk direction model (Preston et al.1989) suggests a positive risk direction when males and females are compared, but a negative risk direction (selective mortality or acquired immunity) operating within males. Yet neither explain the paradox. However, if both selective mortality and acquired immunity were operating along with another direct influence, a male physiological disadvantage, the pattern might be explained. The densely populated environment these people lived in meant exposure to infectious pathogens was a major threat. Males are known to be biologically disadvantaged in terms of infection compared to females, including viral and bacterial pathogens (Klein 2000; Dyson and Gráda 2002; Spolarics 2007). Therefore, males may be more physiologically disadvantaged in this specific environment compared to females. This would explain both the increased likelihood of childhood insults and the higher risk of adult mortality that males experienced. Furthermore, if infectious disease was also a major driver of adult mortality then it may be males with a greater immunological repertoire, gained from previous infectious encounters, who are the least frail males in this context. Therefore, males who experienced more childhood infections, evidenced as hypoplastic defects, were relatively less likely to die younger and able to survive into old age. Thus, in this infectious environment, adult mortality was more selective towards males than females due to a biological male disadvantage, while individual male selection was governed by acquired immunity. Variation in earlier disease exposures resulted in heterogeneous levels of frailty within males which

became evident in older age; those who had survived prior infectious disease were the most robust.

8.3.3 Variation in other adverse health measures

Males and females also differed in their risks associated with severe periodontitis in adulthood. Males who experienced annual health insults, but not females, were at increased risk of severe periodontitis. This positive risk direction was also noted when all individuals were analysed collectively (discussed previously) and correlated environments suggested as the connecting mechanism. The male association suggests that they may be driving the collective association. This sex differential might be a particularly informative feature regarding the nature of the correlated environments. For example, as boys may be more vulnerable in infectious environments (Klein 2000; Dyson and Gráda 2002; Spolarics 2007), they may be more likely to experience regular insults compared to females. In addition, adult males are also more likely to experience periodontitis, although the specific reason is unclear (Grossi et al. 1994; Grossi et al. 1995). The risk direction model (Preston et al. 1998) emphasises the role of social factors operating in correlated environments, as an indirect associational influence, while physiological influences are only considered in terms of scarring. The model could be usefully extended to consider additional physiological factors, such as dimorphic responses to infection, which may act as a continuous influence across the life course.

Growth deficits were the only evident impact of childhood stressors that affected females. Females who had experienced multiple childhood health insults had shorter femora and tibia compared to females with fewer childhood health insults. This would be best explained by a direct factor of physiological scarring, where multiple

physiological insults have resulted in growth deficits. Relatively short femoral and tibial lengths, however, are not always indicative of illness or under nutrition during development. Research investigating growth patterns among Holocene foragers of the South African Cape, who were relatively short-statured as adults, found the tempo and magnitude of growth were similar to that of modern, healthy populations (Pfeiffer and Harrington 2010). The authors conclude that the short stature, including relatively short adult femurs, was not due to pathological processes but adaptive to the environment in which they lived. Nevertheless, in my research, the negative association between femur lengths and multiple hypoplastic defects certainly points to a pathological influence.

Longevity or other health measures, such as periodontitis, were not influenced by early insults affecting females, regardless of their frequency or repetition. A study analysing medieval samples from northern England also found females who died younger, before 25 years, had shorter leg lengths than those who lived longer, while males did not differ (Watts 2011), possibly suggesting that divergent growth outcomes between the sexes is not uncommon. However, female growth is generally considered more canalised than male, suggesting that male bone length is more likely to be impacted by childhood stressors (Smith and Buschang 2004; Tanner 2010; Floyd 2016; although for an alternative view Hermanussen et al. 2001). So it is curious that only female bone lengths appears influenced by early stressors in these samples. One possibility that may explain this concerns the timing of the health insults in combination with differential periods of rapid growth between boys and girls. Growth rates are generally more rapid in girls until approximately four years of age, after which the pace becomes similar to boys until puberty (Tanner 2010:23). As growth processes are more sensitive to disruption during periods of rapid growth (Ben-Shlomo and Kuh 2002; Lynch and Smith 2005), health insults prior to four years might be expected to have

differential impacts on males and females and therefore affect bone length. Furthermore, if children remain in the same environment in which the stressors occurred, catch up growth may not be able to correct the original deficits (Martorell et al. 1994).

8.4 Influence of Socioeconomic status

While childhood risks and adult health outcomes varied between males and females, socioeconomic position also influenced life course associations. Many of the differences in longevity were maintained by groups of higher status individuals from St. Bride's and Chelsea, in whom the beneficial effect of multiple childhood insults was most pronounced. These associations present a negative risk direction, suggesting acquired immunity, rather than selective morality (based on burial records) is likely to be operating. However, even in the lower status groups, St. Benet's and Farringdon, childhood health insults did not pose an obstacle to longevity. Other research has pointed to socioeconomic differences in the relationship between survival and enamel hypoplasia, but it is usually evident as a negative impact on longevity that most disadvantaged the poorer groups (for example, Palubeckaitė et al. 2002; Miszkiewicz 2015). A similar trend, however, is still evident in this research where it is the higher socioeconomic individuals who appear to gain the most benefit. If this relationship is driven by immunological factors of naivety and acquired immunity, as has already been suggested, one might expect the relationship to be evident in lower status groups, as these may represent a greater proportion of rural migrants (Galloway 1985; Landers 1987). However, it is possible that in lower socioeconomic groups additional health stresses may have accumulated across the life course, such as poor diet and increased general exposure to infection. These may have overridden the advantages afforded by

immunological protection from previous disease exposure. The increased risk of chronic health conditions, such as severe periodontitis, in adults from lower status Farringdon may partially support this suggestion.

In some respects, middle to high status Chelsea represents an anomaly. A survival benefit is evident in early adulthood, before 35 years, when those with multiple childhood health insults experienced half the mortality risk. Individuals who died before 35 years also tended to have longer femurs. During this period Chelsea was transitioning from a rural village to a London suburb with a considerable number of people migrating to the newly developed region (Walford 1878; Cowie et al. 2008). The amount of building and construction work required a substantial number of labourers, while the increasing number of middle to high socioeconomic status families moving into the area created an increased demand for domestic servants (Davenport et al. 2011). So the population may have included a high proportion of migrants in addition to wealthier families and whose childhood environments may have been very different. In addition, Chelsea is the only group where periosteal lesions appear connected to childhood insults, specifically multiple hypoplastic defects and healed periosteal lesions. As healed periosteal lesions are suggested to reflect increased survivorship (DeWitte 2014), this association would also point to a negative risk direction and acquired immunity. The presence of migrants in Chelsea raises the possibility of immunologically naïve individuals and may explain why the connection between multiple childhood stressors and surviving past 35 years was most apparent in this parish.

8.5 Variation in influences and health outcomes amongst groups.

It is apparent that the dominant influences operating over the life course varied amongst the groups. Both socioeconomic status and sex mattered in these relationships, which is not apparent when samples are analysed collectively. A summary of early health insults, adult health outcomes, and the likely connecting mechanisms that operated in the various groups are presented in Figure 8.2. In some groups, the influences and outcomes are clear and straight forward, such as the prevailing influence of immunity operating on the collective group, which represent a combination of all individuals from each cemetery sample. When assessed collectively, however, some of the influences operating on specific groups were masked. For example, only female femoral lengths appear strongly influenced by childhood health insults, which as discussed could be related to variation between boys and girls in in the pace of early growth rates. And while in the collective group multiple insults and increased survival past 35 years suggests acquired immunity, in males the impact is mainly evident after 65 years, suggesting that selective mortality was operating over adulthood. Furthermore, in the lower status groups, no particular influences and survival outcomes were apparent, which might possibly be due to conflicting influences operating simultaneously, such as immunological factors, selective mortality, and correlated environments. It is also possible that there were particular periods of vulnerability operating between the ages of two and six years that were influential to these outcomes. Before life course pathways, such as critical periods or stress accumulation models as proposed by Ben-Shlomo and Kuh (2002), can be fully assessed, the relevance of insult timing needs to be considered.

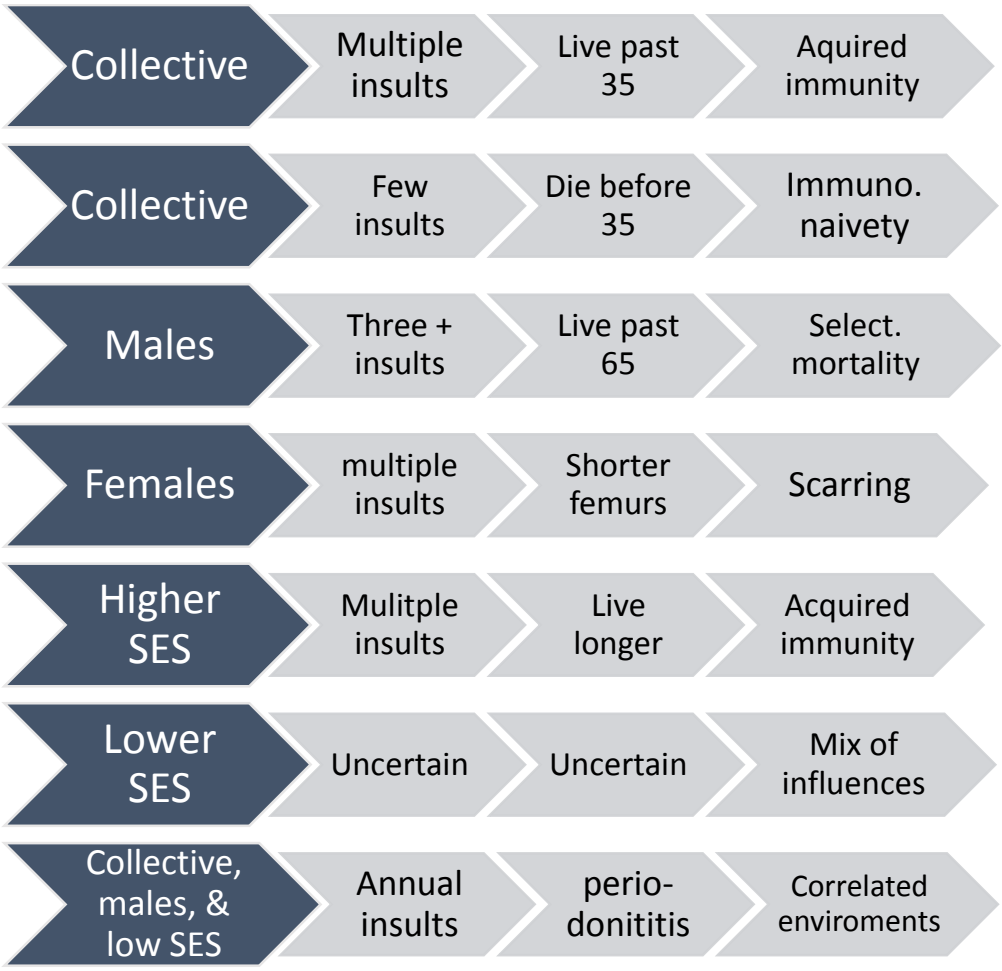

Figure 8.2 Summary of childhood health insults, adult health outcomes, and suggested linking mechanism by assessment groups. SES = socioeconomic status.

8.6 The timing of childhood health insults and critical periods

The series of conceptual life course models proposed by Ben-Shlomo and Kuh (2002), suggest that adverse adult health might result via either a critical period or stress accumulation pathway. So which might be apparent in these individuals from industrialised London? In its strictest sense, a critical period model describes an insult during a specific period of development that results in the structure or function of organs, tissue, or physiological processes being permanently altered (Ben-Shlomo and Kuh 2002). This can be extended to include later life risk factors, which may reveal damage not previously apparent, such as senescence and declines in cellular repair

processes (Paulino et al. 2010), as well as modifiers, such as obesity, that might exacerbate the initial damage (Eriksson et al. 2001). These variants however all involve the original damage occurring with a limited age or development period.

A large body of research suggests that the timing of childhood stressors may be a relevant factor in associations between early and later health outcomes (for example, King et al. 2005; Littleton 2005; Mendez Colli et al. 2009; Temple 2009). Conversely, in this research the role of timing appears ambiguous with no apparent connection to adult survival, unlike the frequency of childhood health insults. In situations when the timing (the age when enamel defects were formed) was significantly associated with outcomes, including femur length and severe periodontitis (Table 8.1), the association was also evident with either annual or multiple insult occurrences. For example, the collective sample, males, and low status Farringdon, all had an increased risk of severe periodontitis if they had experienced annual childhood defects, while females were also more likely to have shorter femur if they experienced at least two childhood health events. The magnitude of risks associated with annual or multiple insult occurrences were consistently greater than they were for timing. This could suggest that it is the repetition of childhood health events that are associated with adverse effects, while timing may be largely incidental. Furthermore, no single age is consistently associated with adverse health outcomes. For these reasons, including the lack of any impact on adult survival, the timing of childhood health insults does not appear relevant in these samples. In contrast, the frequency of childhood health insults, at least that were causal to hypoplastic defects, is associated with increased adult survival and growth deficits, while regular annual insults appear linked to severe periodontitis

Table 8.1 Groups that show significant associations between timing of defects and adverse outcomes.

	Age of occurrence (years)	Adult health outcome
Collective group	4 and 5	Severe periodontitis
Males	2	Severe periodontitis
Females	4	Shorter femurs
Farringdon (Low SES)	2 and 4	Severe periodontitis

The results of this research do not support a critical period model, at least not which was apparent between two and six years of age. However, it could be possible that hypoplastic defects might not register health insults that inflict the type of physiological damage sufficient to reveal a critical period. For example, animal studies suggest that acute infections are more likely to cause linear hypoplastic defects, while chronic condition are not (Suckling et al. 1986). Further, controlled pig studies have shown that in animals largely protected from parasite infection, long term starvation resulted in altered enamel histology and under mineralisation, but not hypoplastic defects (McCance et al. 1968). If chronic conditions, such as under-nutrition, have greater potential to inflict long term damage than acute health insults, then it is possible that these have been missed as contributing factors.

Another issue that could confound these findings is the recording level used to identify hypoplastic defects. Some researchers have concern regarding the arbitrary nature of the lowest recording level used in the macroscopic field recording method (Hillson and Bond 1997; Hassett 2012, 2014; Cares Henriquez & Oxenham 2017), which is based on a defect's tactile characteristic. Specifically, the field method may miss subtle or faint defects. Based on my own observations, I have noticed a tendency

for defects on the mandibular canine to be more prominent in the region of enamel that formed when the maximum number of crowns were undergoing amelogenesis – the mid crown region that forms during the third year of age. If this association is real, it could mean that defects formed at a younger age may be relatively faint and not recorded, yet could still represent a similar level of physiological stress as associated with more apparent defects in the mid crown region. The implication of this is that if a critical or sensitive period is present prior to three years of age, it may well have been missed in my analysis.

8.7 A stress accumulation model

In contrast to a critical period model, the accumulation of risks model considers how risk factors operating over the life course may gradually combine to raise morbidity and mortality risks (Ben-Shlomo and Kuh 2002). These risks might result from separate and independent insults, or may be correlated and cluster in socially determined ways, for example, low socioeconomic position, poor diet, and childhood infections. In addition, they may occur as a chain of risks where one leads to further risks, for example, inability to work due to chronic illness, leading to a poor diet and inadequate housing, which increases the risk of further disease exposure. Stress accumulation models are complementary to the concept of allostatic loading, where the presence of chronic stressors, including both physiological and psychosocial, may result in the accumulation of damage to physiological systems and processes (McEwen 1998). In my results, the association between annual childhood health insults and adult periodontitis is best explained by an accumulation model. For example, the risk direction model (Preston et al. 1998) suggests that correlated environments may explain how these two risks are related, where being male is the commonality that explains both

early and later risks. A critical period model is excluded, as timing is not considered a defining factor in the relationship, which by default points to a risk accumulation model. Whether the accumulation of risks associated with periodontitis are independent, clustering, or a chain of risks, is unclear as there are possibly multiple biosocial factors associated with the disease. Preston et al. (1998) suggest that correlated environments describe indirect associations such as social influences, which in this situation would dictate the linking mechanism reflects gender related factors. However, it is also possible the risks are connected through an increased male (biological) susceptibility to infections, which based on Prestons' et al. (1998) model would be a direct physiological influence. Therefore, it may not always be possible to distinguish between risks maintained by gender related factors (indirect social influences) and those associated with biological sex (direct physiological influences). Furthermore, if the underlying causes of the early and later risks are not known, their relationship to each other may not be able to be established, including whether they are reflect independent, clustering, or a chain of risks.

A risk accumulation model can also account for the relationship between childhood insults and increased adult survival (Ben-Shlomo and Kuh 2002). In this situation, it is possible that the accumulation of disease exposures over childhood allowed survivors to gain a wider repertoire of antibodies, leaving the more immunologically robust to survive London's endemic diseases. Conversely, it is also likely that in lower status groups fewer individuals were able to survive infectious diseases, such as cholera, which disproportionally affected them. The accumulation of risks associated with social inequalities, such as overcrowded housing and inadequate hygiene, along with poorer diet and health care, likely conspired across their life course. This is evident in the higher morality risks for low status children, which would have

resulted in only the more robust individuals surviving to adulthood. This effect may partly explain the similarity between adult mortality risks in the higher and lower status groups. Higher morality in the lower socioeconomic group during subadult years may have had an equalising effect on adult mortality risks. This impact, however, may have been in addition to outward migration of tuberculosis victims, as discussed in chapter six (6.7.2), which may have been more marked in lower status adults. The impact of social inequalities is also evident in how the survival benefit associated with childhood insults was most apparent in the higher status groups; it is likely that in poorer individuals immunological benefits were overridden by other health risks they were exposed to, particularly tuberculosis (Landers 1993).

8.8 Mismatched disease environments

A noticeable theme in these results is that acquired immunity had a marked influence on survival. During this period of increasing urbanisation, certain infectious diseases, such as measles and smallpox, were endemic to London, but not in the rural towns and villages from which many London immigrants originated (Davenport et al. 2011). During the Industrial revolution, it was noted that many labourers moving to London from country towns and villages were more likely to die from infectious disease than native Londoners, who had been exposed to these infections since childhood (Davenport et al. 2011, 2016; Landers 1993:1554-155). The impact is sufficient to be detectable in historical records, where mortality peaks for smallpox often coincide with increased grain prices. The raise in local grain price usually indicates decreased production, resulting in decreased rural employment, culminating in more people moving to London for employment (Galloway 1985). For those who

survived smallpox, however, lifelong immunity was acquired, which is why it offers a useful marker of migrants (Davenport et al. 2011, 2016; Landers 1993). It is also fortuitous that the period of interest, 1783 to 1853, spans a time when smallpox was endemic to London and other large urban centres, but not yet in the smaller or rural regions, from where many migrants originated (Davenport et al. 2011). Later in the 19th century, when smallpox was endemic to the nation, this marker of migration is lost (Davenport et al. 2011). Although smallpox was unlikely to be the only risk, disease or otherwise, faced by new immigrants to London, it provides a useful avenue to investigate migration.

Based on burial records, smallpox was responsible for 7% of burials in the 20 to 35 years age group, most of whom were females of low socioeconomic status. Although this is not a large number of deaths compared to tuberculosis, it is important because it reveals the presence of adults not been previous exposed to the smallpox virus and who, therefore, were most likely migrants. Although smallpox is just one of the many infectious diseases that infected London during the period, it reflects an environment where certain childhood exposures would have been beneficial to subsequent survival. It also suggests that many new migrants were probably younger adults. In the skeletal remains, the direct survival benefit is generally less obvious in females than in males, possibly because these include individuals from all four socioeconomic groups, rather than only St. Bride's and Farringdon, and which may have varied in their composition of male and female immigrants. Furthermore, other diseases in addition to smallpox can provide immunity, such as measles, which are not accounted for in this analysis. Furthermore, measles can be particularly hazardous to susceptible adults (Krause, 1979). For males, the survival benefit operated over early and middle adulthood, when

selective mortality was operating, marking those with more childhood exposures as most likely to live past 65 years.

In essence, these findings point to a mismatch between the disease environment an individual's acquired immune system was prepared for, and the one the individual subsequently moved into. Migrants moving to London entered a different disease environment, with novel pathogens, against which they had no protection. In sum, these results suggest that while an accumulation of stressors acting across the life course disproportionately impacted the health of lower status individuals, other factors not often considered in bioarchaeological studies were also operating, such as immunological naivety and mismatched disease environments. Furthermore, in this particular London environment where infectious disease was a major cause of morbidity and mortality, such as tuberculosis (Landers 1993), males were likely at a slight, but noticeable disadvantage. While the risk direction model (Preston et al. 1998) does not provide for these additional direct physiological (immunological naivety and biological sex dis/advantages) and indirect associational (mismatched disease environments) factors, it could be expanded to include them.

8.9 Extension to risk direction model

The risk direction model, proposed by Preston at al. (1998), might be usefully extended to include more information on the direction of risks as well as additional mechanisms that might operate over the life course. I have broadened the direction of risks from positive and negative risk directions to differentiate between risks that were consistently higher or lower, or shifted from an earlier higher risk to a later lower risks and vice versa (Figure 8.3). This is because the nature of the risks, as well as shifts in direction, allow more information about the nature of the mechanisms to be extracted

from the data. For example, while a shift in risks from high to low might suggest a direct physiological factor is operating, such as acquired immunity, a shift from low to high may be explained by immunological naivety. In addition to indirect association influences, such as selective mortality, a mismatch disease environment might also exert an influence. Risks that remain constant might suggest indirect associational factors, such as correlated environments, but might also point to direct physiological factors, including a male biological disadvantage. These extensions increase the capacity of the model by allowing a greater number of potential influences shaping health outcomes over the life course to be considered and might be helpful in untangling some of the complex biosocial interactions.

	Direction of risks	Direct, physiological	Indirect, associational
Positive	High to high	Physiological advantage	Correlated environments
Positive	Low to low	Scarring, physiological disadvantage	Correlated environments
Negative	High to low	Acquired immunity	Selective mortality
Negative	Low to high	Immunological naivety	Mismatched disease environments

Figure 8.3 Extended version of risk direction model proposed by Preston et al. (1998)

8.10 Evaluation of approaches used and further directions

This work demonstrates how intimately and complexly biology and culture are implicated in human health. Importantly, a life course approach was able to identify situations when some early-life stressors were beneficial to longer term survival, demonstrating that not all childhood insults represent the same threat to subsequent health. It also revealed how adversity in early life can continue across the life course. The influence of early health insults on adult health outcomes depended on biosocial aspects of both environments. Assessing adult health status in skeletal material is difficult, due to the limited range of disease processes that impact bone as well as the frequently ambiguous nature of bony lesions. Thus, insight into adult morbidities is particularly limited. Severe periodontitis, as opposed to the more ubiquitous chronic forms of the disease, however, may prove a useful indicator of adult health status. The condition was most frequent in age groups that would be expected to have higher rates of both chronic disease and mortality rates, the 50 to 64 year age group. Its presence in males and low status individuals was also particularly marked, but more focused research is required before its validity can be firmly established.

Burial data was useful in providing information on causes of death, allowing insight into the disease environment most individuals in the samples would have experienced. It was particularly helpful in demonstrating how groups may be differentially impacted by certain diseases. Importantly, burial records also allowed the potentially confounding influence of selective morality to be better understood, suggesting that in London's infectious environment males may have been disadvantaged. Smallpox burials were used to indicate the presence of migrants, but this does not suggest that smallpox was the only threat to migrants. It would be particularly worthwhile to use stable isotope analysis to test my suggestion that immunologically

naive migrants might be maintaining the association between fewer childhood health insults and decreased adult longevity. For example, oxygen isotopes obtained from dental tissue should be able to differentiate between individuals who spent their childhood in London and those who grew up in other regions.

While this study reinforces that in order to understand health in the past a biocultural framework is most productive, it also demonstrates how complicated those interconnections can be. The risk direction model (Preston et al. 1998) offers a useful way to think about relationships, providing a framework to identify dominant influences operating in different groups. How these risks might shift over the life course can point to the nature of the mechanism connecting early and later risks factors. An extension to Preston et al.'s (1998) risk direction model was suggested that considers the nature of shifts in risk directions as well as additional influences, such as mismatched disease environments and sexually dimorphic responses to infection. Another consideration is that both direct and indirect factors may be operating together or at different times over adulthood so linking mechanisms might not fall decisively into a single category.

In this analysis, only health insults experienced between two and six were considered, as my focus was on childhood risk factors and how they might impact adulthood. However, it would be useful to analyse the hypoplastic defects in those who failed to survive to adulthood and test some of my suggestions regarding survival. For example, if some adults are advantaged by having experienced multiple health insults in childhood, is this pattern also evident in older children and adolescence or is it only evident in adults due to most migrants being young adults? In addition, the skeletal samples were selected for this analysis to represent a socioeconomic gradient, where a graded response in health stressors and outcomes might be apparent. While this might be a useful approach if larger samples were able to be obtained, results may have been

clearer if only the two extreme socioeconomic groups, high status St. Bride's and lower status Farringdon, had been focused on. Particularly as these two groups have a wealth of historical burial data, allowing greater insight into factors that influenced mortality. By analysing adults and subadults from these two collection a more detailed account of impacts operating over the life course might be possible.

8.11 Conclusion

At the outset of this research, I expected the age when childhood insults were experienced to likely influence adult health outcomes. My data, however, demonstrated not the effect of timing, but the impact of migration and a mismatch between developmental and later immunological environments. The finding, however, that mismatched environments exerted a significant influence on later health outcomes should not have been surprising as the concept is well known and researched (for example von Hertzen 2000; Barker 2004; Gluckman et al. 2005; Hoffjan et al. 2005; Kuzawa and Quinn 2009; Sironi and Clerici 2010; McDade et al.2016), and intimately tied to the role insult timing. This research does not exclude the notion that insult timing during childhood might negatively influence later health outcomes, but rather suggests that in this context, specific to London during the industrial revolution, its influence on longevity was possibly inconsequential compared to immunological competence. The people in my samples lived during a period of rapid and extensive change to previous life-ways. A period when the rural based economy was superseded by large scale industry, initiating urbanisation at a rate that city infrastructures could not keep pace with. Furthermore, London's growth was largely maintained by immigration. The scale of this migration was such that it has been suggested London acted as a break on the general population growth of England at the time (Landers 1993; Davenport 2011). The

pull of migrants from outlying areas and the high mortality rate amongst immigrants conspired to ensure a constant stream of people entering the city destined for abbreviated lives.

The story told by this analysis was based on both historical and skeletal evidence, and is specific to a single time period and location. However, it has useful implications for bioarchaeology regarding that impact of migration and could possibly suggest a signature that would be apparent without additional historic data. For example, a mark of endemic disease is that infections are focused in young children, such as measles, smallpox, and chickenpox (amongst many) as these represent the susceptibles within a population (Davenport et al. 2011). So, where hypoplastic defects are ubiquitous and higher frequencies are not connected with decreased survival in adults, it could suggest substantial movement of people from regions with low rates of infectious disease into a regions with higher rates or endemism. In addition, this research suggests that not all health insults have a negative impact on adult health and survival, but in certain situations may be beneficial. However, it will depend on the main causes responsible for the hypoplastic defects. For example, in environments where malaria is a major threat, it is possible that multiple childhood infections will only exert a survival deficit in adulthood, due to organ damage that repeated attacks can incur in childhood (Robinson et al. 2006; Taylor et al. 2012). The nature of long term impacts depend on the specific biological and cultural context, nevertheless these processes are identifiable.

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APPENDIX ONE: A METHOD TO ESTIMATE ORIGINAL CROWN HEIGHT IN WORN MANDIBULAR CANINES

Abstract

This study investigates whether original crown height (OCH) can be accurately estimated in worn mandibular canines using a regression equation based on ratios of worn crown height and a linear measurement of exposed dentine taken along the midline of a tooth. Being able to accurately estimate OCH has several benefits: first, in analyses where OCH is required, it may allow worn crowns to be included in assessments that would normally have been excluded. Second, the percentage of crown height lost to wear, as well as the percentage of crown height remaining, can be quantified for individual crowns, thus allowing more accurate positioning of crown height deciles.

Thirty human mandibular canines from a modern New Zealand population were sectioned longitudinally and imaged under low level microscopy. This allowed worn cusps to be reconstructed. On these images, ratios of crown height along with dentine thickness were recorded on variably worn teeth at each half decile increment of OCH. Additionally, the decile position of the tip of the dentine horn was recorded to investigate its usefulness as a landmark.

Results suggest that a log10 transformation of the ratios allows a cubic regression curve to best describe the relationship between these ratios and crown height deciles ($R^2 = 0.995$, $p < 0.005$, df1=3, df2 = 315). Furthermore, the apex of the dentine horn was found to typically lie between 0.6 to 1.0 deciles beneath the original crown height maxima in this sample. A good degree of concordance was found (r=0.97, *p*

<0.005, *n*=11) between this method of estimating original crown height and estimations based on reconstructed crowns.

Introduction

Linear enamel hypoplasia are a commonly recorded nonspecific stress indicator, evident on teeth as a horizontal groove or greater than expected spacing between perikymata (Hillson 1996). The defect's location on the crown relates to the individual's age when they experienced the causal stressors, which are often attributed to synergisms between under-nutrition and disease (Goodman and Rose 2000). Ageing charts based on histologically derived ages associated with crown height deciles, developed by Reid and Dean (2000; 2006) provide a useful way to estimate the age of the individual when the defects formed. The accuracy of these age estimations, however, depends on correct assessments of original crown height. This can be difficult in worn crowns.

The aim of this investigation is to identify and evaluate how consistently dentine thickness covaries with the progressive loss of crown height in mandibular canines as well as identifying where the apex of the dentine horn is typically positioned. This research builds upon previous work (McFarlane 2013) where coronal dentine was found to increase in thickness (from dentine horn to cervix) in a particularly consistent manner, regardless of tooth size, while enamel thickness was more variable. This suggested dentine thickness may have potential as a covariate in predicting the height lost in worn canine crowns. Here I investigate how ratios of dentine thickness and worn crown height might be used to estimate the amount of original crown height missing in worn mandibular canines.

The rationale behind this investigation is based on a simple observation: as crowns becomes progressively worn, the amount of dentine visible on the occlusal surface increases simultaneously with decreasing crown height. Therefore, a regression formula might adequately describe how these ratios change along the length of a crown, allowing prediction of the percentage of original crown height lost to wear, and by extension, the percentage of crown remaining. As these ratios are dependent on dentine exposure, it is important to find a method to reliably quantify wear occurring prior to dentine exposure. Consequently, I also assess where the apex of the dentin horn most commonly lies beneath the cusp (as a percentage of original crown height), as well as how variable this position is. To check the usefulness of the proposed techniques, concordance between crown-height estimates obtained using this techniques (i.e. for exposed and unexposed dentine) are tested against estimates from reconstructed cusps of the same crowns using a method described below.

Materials and Methods

The sample consists of 33 permanent mandibular canines extracted from modern New Zealanders as part of routine dental procedures. Subsequently these teeth were collected by Dr RMS Taylor and donated to the Anthropology Department, University of Auckland. No personal information, such as age or sex, was available. Teeth were selected with varying degrees of wear depending on their purpose within the investigation. Unworn to minimally worn crowns, i.e. wear score of 1 or 2 (Smith 1984), were used for thin sectioning (n =19) while crowns ranging from unworn to moderate dentine exposure i.e. wear score of 1 to 4 (Smith 1984) were used in visual assessments of cusps of intact crowns (n=14), as well as to trial this method (n=11). For

the purpose of this study, loss of crown height is referred to as wear, without implying a particular causal process (i.e. attrition, abrasion or erosion).

The final goal of this study is to produce a method that can be applied to intact teeth, without cross-sectioning or requiring microscopy but in order to understand the relationship between dentine thickness and crown height, I first needed to assess dentine morphology in sectioned crowns. Principally, this procedure involves assessing worn crown height and exposed dentine thickness in series along the midlines of sectioned crowns as well as the position of the dentine apex beneath the enamel cusp. Worn crown height and dentine thickness measurements are then converted to ratios and plotted so a regression equation can be calculated that best describes the curve. An equation that adequately captures the consistent pattern of change in ratios along the crown should ultimately allow height (in terms of percentage, or deciles, of original crown height) at any given point along the crown midline to be calculated using only two covariates (dentine thickness and worn crown height). To check the efficacy of this method on intact teeth and without microscopy, I estimate crown height on unsectioned crowns and compared these against height estimates for the same teeth after their crowns have been sectioned and cusps digitally reconstructed.

Determining ratios

This phase involved measuring worn crown height and dentine thickness. Thin sections were cut along the crown midline of 19 mandibular canines and produced using standard methods outlined in McFarlane et al. (2014). All sections were cut using a Buehler slow speed saw fitted with a diamond wafer blade. These were then imaged under transmitted light microscopy (Leica MDR) at 25X magnification and micrographs used to create montages of the sectioned crowns in Inkscape software

(Free Software Foundation Inc.). All images were taken so the camera lens was parallel to the midline of the crown. As these sections were cut along the crown midline, measurements are effectively taken along this dimensional plane. Ratios were calculated from measurements of dentine thickness and crown height, assessed at each half decile of original crown height using ImageJ open source software (version 1.5), see Figure 1. Because ratios describe relative proportions they are unaffected by the unit of measurement, so pixels were used as the measurement unit. This minimizes additional error associated with converting pixels to millimeters. The cusps of crowns with even the slightest wear were reconstructed digitally using a Bezier curve function to follow the natural extension of labial and lingual crown curves. This procedure recreates the original cusp outline and is based on the methods described in Saunders et al. (2007) and Guatelli-Steinberg and Reid (2010).

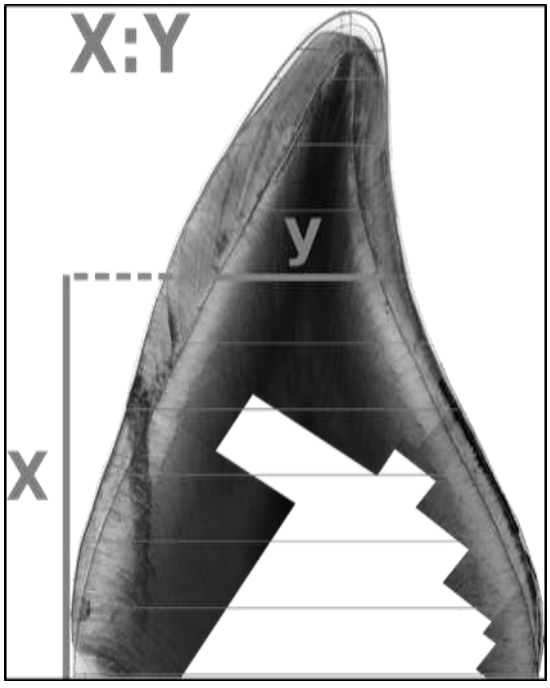

Figure 1 Crown in cross section showing linear assessments of dentine thickness (Y) and corresponding crown height worn to height (X). A ratio value at X is obtained by as X/Y. Horizontal line mark deciles, rather than half deciles that were used in actual assessments.

Location of dentine horn apex

An approach is developed to estimate crown height when cusps were slightly worn but dentine was not exposed, or only minimally exposed, as in these situations ratios cannot be calculated so alternative criteria are needed. In particular I wanted to know the upper and lower extents of dentine apex position and how consistent it might be considering variation in tooth size. In addition to recording dentine apex position on micrographs of thin sectioned crowns (n = 15) with complete dentine horn apices, intact crowns (n = 9) with minimal wear were also assessed. The following visual criteria was used to define stages of cuspal wear.

1. When no dentine was exposed, the visibility of dentine beneath the occlusal enamel was noted. This is often observable as an area of darker colour, usually yellowish, in contrast to the surrounding enamel but which varies in size and intensity depending on the depth of enamel lying above it.

2. When dentine was exposed, it was recorded based on the amount of exposure. For example, whether a 'pin prick' i.e. < 0.50 mm, or a larger area was exposed.

When dentine was exposed, it was necessary to ensure that actual dentine was assessed and not the dimension of the wear cavity, which due to the sloping enamel edges, can over-estimate the extent of dentine. These observations were compared to dentine apex measurements (vertical depth measured in deciles) taken on the same crowns after being half sectioning along the midline and the surfaces photographed using a Canon EOS 1000D SLR camera.

Approach to curve fitting and estimating original crown height

Once ratios per half-decile of crown height were estimated for 19 mandibular canines using the method just described, several parametric curves were fit. A cubic regression (Equation 1) provided the best fit judging from the percentage of variance in deciles accounted for and the distribution of residuals. All statistical tests were conducted using IBM SPSS (version 20).

Equation 1: $\mu = \alpha + \beta_1(\text{ratio}) + \beta_2(\text{ratio}^2) + \beta_3(\text{ratio}^3) + \varepsilon$

The output of this equation provides an estimate of the amount of missing crown height in terms of deciles. For example, an output of 2.5 in deciles suggests that 25% of original crown height has been lost to wear, therefore 75% must be remaining (Equation 2).

Equation 2: $1 - 2.5_{\text{Decile}} = 7.5 * 100.$

If the height remaining of the worn crown is measured in millimetres then the original crown height can be estimated in the same unit (Equation 3).

Equation 3: $(8.2\text{mm}_{\text{(worn crown height)}} / 75_{\text{(\% crown remaining)}}) * 100 = 10.93\text{mm}.$

The same formulae applies to deciles of missing crown height estimated from the visual assessments.

Trial

To check how well the method could predict missing crown height and estimated original crown height in practice using intact crowns, 11 crowns were selected to be assessed separately. As cusps would likely need some reconstruction, only those with less than a wear score of 3 (Smith 1984) were used to minimize possible error associated with cuspal reconstruction. These crowns were first photographed on a measuring cradle to include labial and cuspal aspects, with each surface parallel to the lens. Measurements were then taken on enlarged images using ImageJ software. For crowns with exposed dentine, worn crown height was measured along the midline from the cementoenamel junction to the edge of the cuspal wear facet. Dentine was also measured along the midline from the most lingual to the most labial extent. All measurements were orthogonal to the plane of interest. Where no dentine was exposed, the visual assessment method was used. After converting ratios to deciles using the regression equation, the crowns were sectioned and imaged so cusps could be reconstructed in order for original full height to be established. The degree of concordance between the two techniques was calculated using Pearson's product-moment correlation coefficient.

Intra observer error

As this method involves a novel approach, it is important to ensure that measurements are reliably repeatable. Therefore, measurements of exposed dentine and crown height were taken on photographic images of twenty randomly selected mandibular crowns with exposed dentine. I recorded the second assessment approximately eight months after the first recordings. Pearson product moment correlation coefficient are used to assess the degree of variation between the sets of

measurements. In addition, raw measurements were converted to estimations of missing crown height in terms of deciles to see if error is minimised when converted to crown height deciles. This is likely as dentine and crown height are measured on a sub millimetre scale and then converted to a considerably larger scale of measurement (deciles), which is likely to render apparent differences at the sub millimetre level inconsequential in terms of crown height deciles.

Person's correlation coefficient suggest a strong correspondence between my first and second set of measurements for dentine ($R = 0.962$, $p < 0.001$, $n=20$) and crown height ($R = 0.817$, $p < 0.001$, $n=20$). The assessments of crown height were slightly more error prone. This is likely because determining the precise occlusal extend of enamel, or where it meets the exposed dentine, can be difficult at times due to curvature of the enamel surface at this point. However, when dentine and crown height measurements are converted to ratios, this variability of minimised, producing a strong correlation between the two sets of values: $R = 0.948$, $p < 0.001$, $n = 20$. When ratios are converted to estimations of missing crown height in terms of deciles, error is further reduced ($R = 0.980$, $p < 0.001$, $n=20$) suggesting only 4% of variation is unaccounted.

Results

Ratios

As expected, ratio values became increasing small from cusp towards the cementoenamel junction, reflecting the increasing thickness of dentine in a cervical direction (Figure 2). The range of values for the first decile reflect the variation in dentine tip position, specifically those in which the tip lay very close to the first decile marker. Overall, the range of ratios became increasing narrow. After the first few

deciles they exhibited only minor variation - as evident by the coefficients of variation, table 1. Importantly, ratio values greater than 45 at the first decile were only associated with crowns where the apex of the dentine horn lay on or very close to this increment. Due to the particular regression curve, equation based estimates using these particular ratios will be in error but instead can simply be assumed as representing 1 decile of missing crown height.

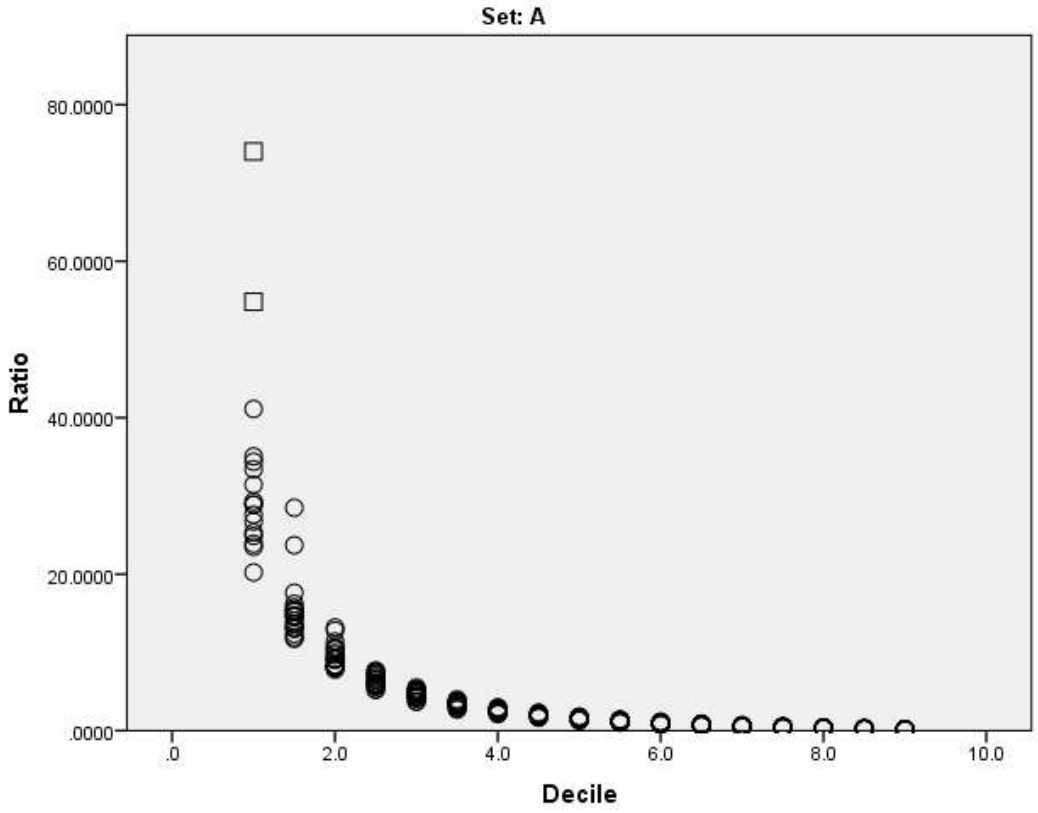

Figure 2 Decay curve of plotted ratio by half deciles. Square symbols in decile 1 have ratio >45 (n=19).

Table 1 Mean ratios, standard deviations and coefficients of variation at each half decile assessment. Decile 1 n = 15 (Excludes crowns with no dentine exposure), all other deciles n = 19.

Decile	Mean ratio	Std. Deviation	Coefficient of Variation
1.0	28.974	5.403	18.6
1.5	15.521	4.100	26.4
2.0	9.598	1.567	16.3
2.5	6.465	0.784	12.1
3.0	4.643	0.520	11.2
3.5	3.397	0.341	10.0
4.0	2.552	0.213	8.4
4.5	1.953	0.158	8.1
5.0	1.518	0.133	8.8
5.5	1.189	0.119	10.0
6.0	0.937	0.100	10.7
6.5	0.735	0.081	11.1
7.0	0.577	0.064	11.0
7.5	0.447	0.048	10.7
8.0	0.340	0.035	10.3
8.5	0.246	0.024	9.9
9.0	0.160	0.016	10.0

Curve estimation

Figure 3 shows the results of a cubic regression fit to the log10-transformed ratios from x number of teeth assessed per half-decile of available enamel (Estimated Decile: Constant = 5.880; β_1 = -4.572, β_2 = -0.174, β_3 = 0.730). This model demonstrated a very good fit across the range of available data and the predicted curve (R^2 = 0.995, p <0.005, df1=3, df2 = 315). Furthermore, little autocorrelation was apparent in the residuals (Figure 4).

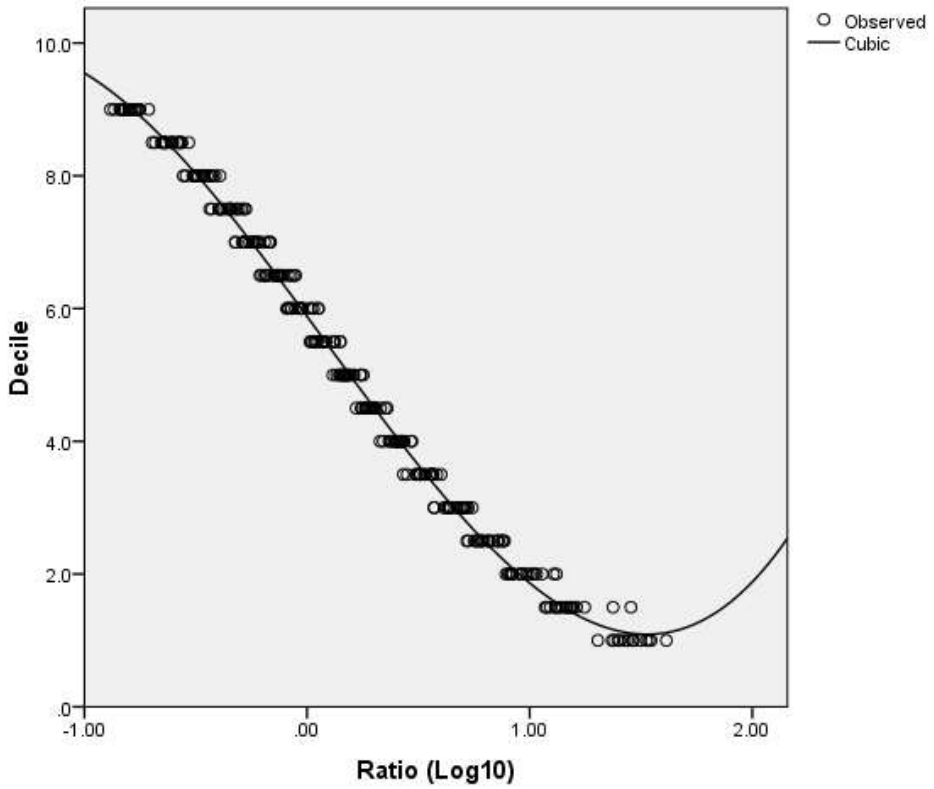

Figure 3. Cubic regression estimates of decile fit to Log10 transformed decile ratios computed per half decile.

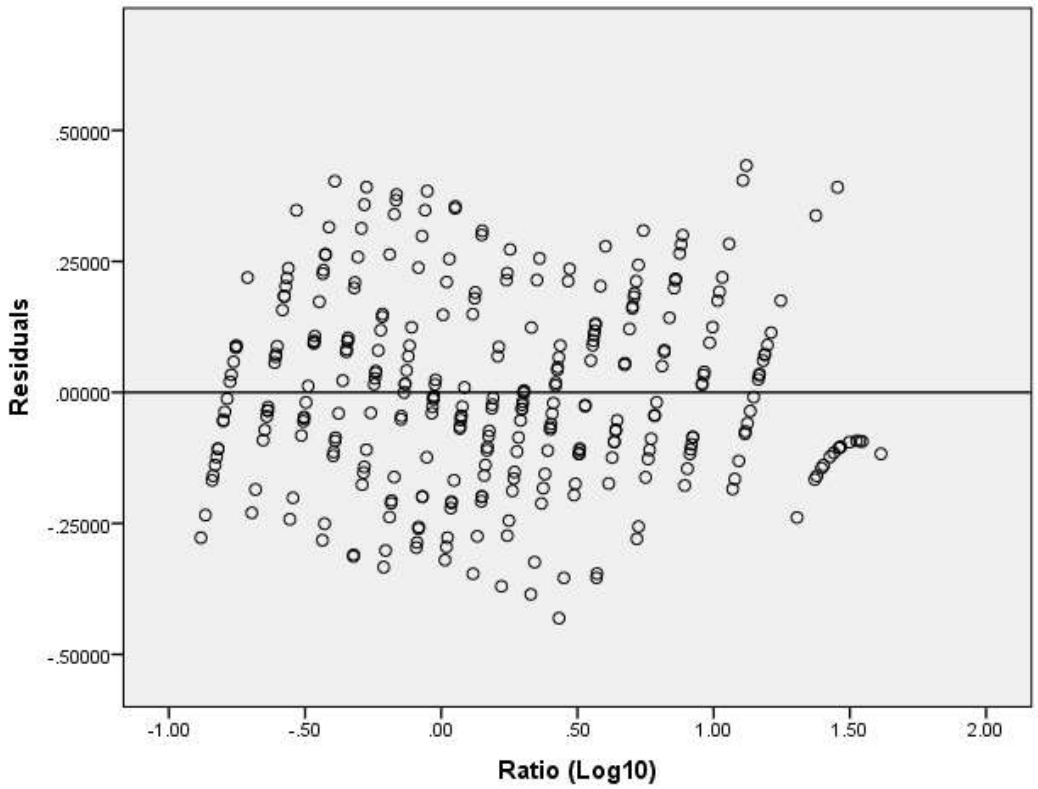

Figure 4 Residuals of log10 transformation of ratio values

Dentine horn apex position

In the 24 canines evaluated in terms of the dentine apex position, the apices of the dentine horn were positioned between 0.6 and 1.0 of the first decile. In other words in no mandibular crown was the apex positioned within the first 0.5 decile of original crown height or significantly greater than 1 decile. However, four crowns evaluated had apices that were at 0.6 deciles and two more were at the 1.0 decile depth. Descriptive statistics are shown in Table 2. Assessments were recorded to the closest 0.5 decile increment, suggesting that in most mandibular canine crowns the dentine apex is positioned between approximately 6.25% and 7.25% of crown height. Furthermore, the position of the dentine apex does not appear to be associated with overall crown height

(Pearson's correlation r = -.148, p = 0.461, n = 24), suggesting that the position of the tip is not influenced by crown size.

Table 2 Descriptive statistic for position of dentine apex within decile 1 for mandibular canines (n= 24). Assessments are in deciles. SD = standard deviation, IQR = inter quartile range

Mean	SD	Median	Mode	Min-max	IQR
0.74	0.12	0.70	6.5 & 7.0	0.6 – 1.0	0.40 (.15)

In crowns with only minor wear facets but no dentine exposure, the tip of the dentine horn is sometimes visible under the cuspal enamel. The appearance of the dentine apex is related to its proximity to the worn cuspal surface and thereby suggestive of the amount of wear that had occurred. Table 3 shows the amount of missing crown height associated with the appearance of the dentine in the visual assessment of nine intact crowns with minimal wear. Crowns can vary in the translucency of their enamel and the estimated apex position may be influenced by this, so criteria is only an approximate guide.

Table 3 Visual assessment of unexposed dentine on canine cusp and associated estimates of lost crown height as fraction of the first, or most cuspal, decile.

Visual assessment of dentine apex position	
No dentine visible through enamel	<0.5 decile
Dentine visible but not exposed	0.5-0.7 decile
Dentine tip just exposed	>0.7 -1 decile

Trial

Table 4 shows the comparisons between my proposed system for estimating original crown height and estimates based on cusps reconstructed in Inkscape. Both sets of estimates have been obtained using the same teeth. The system first requires a visual

assessment of the cusp to determine if dentine is exposed; if not, the visual assessment method is used. If dentine is exposed; ratios are calculated, transformed (log10) and the cubic regression equation is applied to determine the percentage of crown height missing so full crown height can be calculated in millimetres. If the ratio calculated was greater than 45, one decile is estimated to be missing. Pearson's correlation coefficient suggests strong agreement between the two sets of estimates (r=0.97, p <0.005, n=11). A paired t test evaluating the mean difference between the two methods of estimation shows differences were not statistically significant (-0.075 ± 0.31 mm; t = -0.795, df = 10, p = 0.45). No consistent bias towards over or under estimation was evident. This suggests that the minor differences between the two assessments of crown height are mostly due to random measurement error rather than reflecting real or systematic differences.

Table 4 Comparison of crown height estimations for reconstructed cusps and the proposed system. Ratio refers to technique based on ratios of dentine and worn crown height, Visual refers to visual assessment where no dentine is exposed, and R/V refers to crowns where ratios were calculated to be over 45 - so 1 decile was used

Crown height (mm)			
Cusp reconstruction	*Proposed system*	*Δ (mm)*	*Technique used*
13.53	13.33	0.20	Ratio
10.85	11.03	-0.18	Visual
12.18	11.95	0.23	Visual
10.67	11.23	-0.56	Visual
13.43	13.61	-0.18	Ratio
10.05	9.83	0.22	R/V
12.23	12.31	-0.08	Ratio
10.99	11.40	-0.41	R/V
12.25	12.73	-0.48	Ratio
12.07	11.95	0.12	visual
9.62	9.32	0.30	Ratio

Discussion

A novel system to determine the amount of height lost in worn mandibular canines was presented. Crown height estimates obtained using this method are very similar to estimations based on cusp reconstruction. The mean difference of -0.075 mm (95% CI from -0.28 to 0.13 mm) is likely similar to measurement error associated with crown height assessments using digital callipers (see Kieser et al. 1990). Although I am effectively comparing two different methods of estimating original crown height, I suggest my method is comparable to cusp reconstructions, which is an accepted technique for estimating the original extent of cusps with only minor wear (for example, Saunders et al. 2007; Guatelli-Steinberg and Reid 2010). An advantage of my system is it permits an objective method to estimate the extent of wear. The technique should also allow greater accuracy for ageing methods that depend on original crown height in calculations. In situations where crowns are worn, researchers often use a mean value based on unworn crowns in their sample; this technique may therefore allow more effective capture of information linked to individual variation.

The main challenge envisaged in applying the ratio method to worn teeth concerns complications arising from variation in wear slopes. Cusps do not usually wear in a strictly horizontal manner. In the case of the mandibular canine, they tend to slope labially. In these situations, it is important to note that all assessments must be taken at the midline of the crown and to ensure that worn crown height is measured to the edge of the dentine, i.e. where the most cuspal extent of enamel meets the exposed dentine at the midline. As dentine thickness is measured across the midline (labial to lingual), there is a danger that this length could be over-estimated in crowns steep wear

slopes. In these situations, crown height will be slightly under-estimated. The degree to which it will be in error is dictated by the angle of the slope and the amount of dentine exposed: the greater the angle and the more dentine involved – the greater the error. It should be possible to determine a correction factor based on these two variables, but this has not yet been investigated.

This method was developed using a relatively small sample of teeth from New Zealand, so I cannot be sure that all the variation in dentine morphology was captured. Nor is it possible to comment on how this may vary among other populations, though these are important issues worthy of further investigation. However, it is interesting to note that neither the dentine apex position nor ratios appeared to be influenced by crown size. In an earlier study it was found that dentine morphology showed considerable less variation than enamel, especially when tissue thicknesses were assessed along the length of a canine crown (McFarlane 2013). This may suggest that dentine morphology is more constrained. In this sample, the dentine apex positions ranged from 0.6 to 1 decile of crown height. However, crowns with advanced wear i.e. greater than a wear score of 4 (Smith 1984), were not used to investigate apex positions due to possible error associated with cusp reconstruction. So although I cannot be certain that no mandibular canine apex will be positioned in the second decile, I can suggest that they are more likely to be positioned within the first 10% of original crown height. Notably, it was found that ratios with a value greater than 45 only occurred when only very minor wear of the dentine tip had occurred. This is important to be aware of because such a ratio will yield an incorrect cubic regression product. However, it is simply remedied by assuming one decile has been lost.

Generally, ratios values appeared stable. These showed the greatest variation within the most cuspal deciles due to variation in to the dentine tip position and became

increasingly smaller along the crown. From the fourth decile onward very little variation between ratios was apparent. The consistency of both dentine tip positions and ratios, regardless of crown size, also supports the use of deciles as a meaningful unit of measurement, allowing specific locations on crowns (e.g. a defect at decile 5.5) to be comparable to the same position on another crown.

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APPENDIX TWO: CALCULATIONS FOR BAYESIAN AGEING

The procedure for calculating posterior probability, as described by Gowland and Chamberlain (2002), are displayed below. First, this involves the distribution of trait scores with known age group are shown (Table A). Next Table B shows the likelihood of a trait, given known age, P(T|A). These values were then multiplied by the prior probability from the life table probabilities of death, $P(T|A) \times P(A)$, which produces the overall probability of possessing a particular indicator state given the prior (Table C). The posterior probabilities are calculated by dividing each probability of trait, given age (Table C cell values) by the total portability for each score.

Table A: Distribution of trait scores with known age groups for each individual

		Age groups			
	score	20-34	35-49	50-64	65+
Auricular surface (Lovejoy et al. 1985)	1	0	0	0	0
	2	2	0	0	0
	3	1	1	1	0
	4	0	3	3	0
	5	0	2	5	2
	6	0	1	3	0
	7	0	0	3	4
	8	0	0	1	0
	Total	3	7	16	6
Pubic Symphysis (Suchey – Brooks)	1	1	0	0	0
	2	1	0	0	0
	3	0	1	1	0
	4	0	1	0	0
	5	0	3	5	3
	6	0	0	0	0
	Total	2	5	6	3
Canine Wear	1	2	0	0	0
	2	2	10	10	4
	3	0	1	4	1
	4	0	0	3	4
	Total	4	11	17	9

Table B: The probabilities of trait, given known age, P(T|A)

		Age groups			
	score	20-34	35-49	50-64	65+
Auricular surface (Lovejoy et al. 1985)	1	0	0	0	0
	2	0.67	0	0	0
	3	0.33	0.14	0.06	0
	4	0	0.43	0.19	0
	5	0	0.29	0.31	0.33
	6	0	0.14	0.19	0
	7	0	0	0.19	0.67
	8	0	0	0.06	0
Pubic Symphysis (Suchey – Brooks)	1	0.50	0	0	0
	2	0.50	0	0	0
	3	0	0.20	0.17	0
	4	0	0.20	0	0
	5	0	0.60	0.83	1.00
	6	0	0	0	0
Canine Wear	1	0.50	0	0	0
	2	0.50	0.91	0.59	0.44
	3	0	0.09	0.23	0.11
	4	0	0	0.18	0.44

*Table C: Overall probability of possessing a particular indicator state given the prior [P(T|A) *P(A).*

		Age groups				
	Score	20-34	35-49	50-64	65+	Total
Auricular surface (Lovejoy et al. 1985)	1	0	0	0	0	0.00
	2	0.12	0	0	0	0.12
	3	0.06	0.04	0.03	0	0.13
	4	0	0.13	0.09	0	0.22
	5	0	0.09	0.16	0.33	0.58
	6	0	0.04	0.09	0	0.14
	7	0	0	0.09	0.67	0.76
	8	0	0	0.03	0	0.03
Pubic Symphysis (Suchey – Brooks)	1	0.09	0	0	0	0.09
	2	0.09	0	0	0	0.09
	3	0	0.06	0.08	0	0.14
	4	0	0.06	0	0	0.06
	5	0	0.18	0.42	1.00	1.60
	6	0	0	0	0	0.00
Canine Wear	1	0.09	0	0	0	0.09
	2	0.09	0.28	0.29	0.44	1.11
	3	0	0.03	0.12	0.11	0.26
	4	0	0	0.09	0.44	0.53